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Proposed Re-evaluation Decision PRVD2017-19

Fosetyl-aluminum and Its Associated End-use Products

Consultation Document

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Proposed Re-evaluation Decision

Under the *Pest Control Products Act*, all registered pesticides must be regularly re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they continue to meet current health and environmental safety standards and continue to have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports, and other regulatory agencies. The PMRA applies internationally accepted risk assessment methods as well as current risk management approaches and policies.

Fosetyl-aluminum (fosetyl-Al) is a fungicide used to manage various diseases on a wide range of agricultural crops, ornamentals and turf. Fosetyl-Al is applied as a drench treatment and foliar spray by ground application equipment. It is registered for commercial use only.

This document presents the proposed regulatory decision for the re-evaluation of fosetyl-Al including the proposed risk mitigation measures to further protect human health and the environment, as well as the science evaluation on which the proposed decision was based. All products containing fosetyl-Al registered in Canada are subject to this proposed re-evaluation decision. This document is subject to a 90-day public consultation period, during which the public, including manufacturers and stakeholders, may submit written comments and additional information to the PMRA. The final re-evaluation decision will be published taking into consideration the comments and information received.

Outcome of Science Evaluation

Fosetyl-Al provides control of various fungal diseases, mainly damping-off, root rot and downy mildew on a wide range of agricultural crops as well as on ornamentals and turf. Fosetyl-Al has a low risk for developing resistance in fungal diseases. It can be used in rotation with other mode of action fungicides, including fungicides that are at high risk for developing resistance, to help delay resistance development. In addition, fosetyl-Al is approved for use on ornamentals for the management of sudden oak death disease, a quarantine pest regulated in Canada.

With respect to human health, risks of concern were identified for certain occupational exposures to fosetyl-Al, resulting in the proposal to cancel uses on cut flowers and drench application to bedding plants. Additional mitigation measures are proposed for some of the remaining uses, including longer restricted-entry intervals (REIs). Exposure from these remaining uses is unlikely to affect human health when used according to the proposed label directions.

Fosetyl-Al enters the environment when used outdoors. It is unlikely to affect the environment when used according to the proposed label directions, which include advisory statements and spray buffer zones.

Proposed Regulatory Decision for Fosetyl-Al

Under the authority of the *Pest Control Products Act* and based on the evaluation of currently available scientific information, the sale and use of products containing fosetyl-Al in Canada are considered acceptable for continued registration. However, additional risk mitigation measures are proposed on product labels to further reduce risks associated with human health and the environment, including longer REIs on some crops, the cancellation of certain uses, and buffer zones.

Human Health

To protect mixers, loaders and applicators, the following measures are proposed:

- Prohibit the use of fogging equipment (handheld or automated) or handheld mistblowers.
- Increase the minimum spray volume and the level of personal protective equipment when applying with a mechanically pressurized handgun to blackberries, raspberries and strawberries.
- Limit the amount handled for use of wettable powder product(s) on turf to no more than 320 kg fosetyl-Al per person per day.
- Wear a chemical-resistant hat for airblast applications.

To protect workers entering treated sites, the following measures are proposed:

- Cancel the use on cut flowers.
- Increase REIs for apples, blackberries, highbush blueberries, red/black raspberries, grapes, brassica leafy vegetables, onions, spinach and ornamental plants.
- Cancel drench applications to bedding plants.
- Establish a minimum 12-hour REI for other crops where appropriate.

To clarify the registered use pattern, the following measure is proposed:

- Add a label statement indicating that products are not to be used on residential turf such as residential lawns, gardens, playing fields, cemeteries, and schools.

Proposed residue definition:

- The current residue definition for fosetyl-Al is "aluminum tris[ethyl phosphonate]" for enforcement purposes. No change to the residue definition for enforcement purposes is proposed. For risk assessment purposes, combined exposures to both fosetyl-Al and its metabolite phosphonic acid, expressed as "aluminium tris(ethyl phosphoate)", are considered.

Environment

The following measures are proposed:

- Advisory statements to inform users that fosetyl-Al can be toxic to non-target organisms including beneficial arthropods, birds, mammals, and aquatic species such as amphibians, freshwater fish, oysters and marine algae.
- Advisory statements to inform users of conditions that may favour run-off and leaching.

- Spray buffer zones to protect aquatic habitats from drift.

International Context

Fosetyl-Al is currently acceptable for use in member countries from the Organisation for Economic Co-operation and Development (OECD), including Norway, Australia and the United States. No decision by an OECD member country to prohibit all uses of fosetyl-Al for health or environmental reasons has been identified at this time. Fosetyl-Al is under registration review at the United States Environmental Protection Agency (USEPA).

Next Steps

The public, including manufacturers and stakeholders, are encouraged to submit additional information that could be used to refine risk assessments (exposure data or use information) during the 90-day public consultation period upon publication of this proposed re-evaluation decision.

All comments received during the 90-day public consultation period will be taken into consideration in preparation of re-evaluation decision document, which could result in revised risk mitigation measures. The re-evaluation decision document will include final re-evaluation decision, the reasons for it and a summary of comments received on the proposed re-evaluation decision with the PMRA's responses.

Science Evaluation

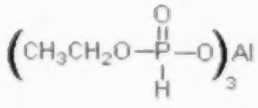
1.0 Introduction

Fosetyl-aluminum (fosetyl-Al) is a systemic fungicide that belongs to the Resistance Management Mode of Action Group Number 33 (phosphonates). The mode of action of fosetyl-Al is not fully understood, but it is suggested that it acts by inhibiting spore germination and by blocking mycelial growth and sporulation. Fosetyl-Al is rapidly absorbed by leaves and roots and has unique characteristics in terms of both upward and downward movement inside the plants.

Following the re-evaluation announcement for fosetyl-Al, the technical registrant and primary data provider in Canada indicated continued support for all uses included on the labels of end-use products.

2.0 Technical Grade Active Ingredient

2.1 Identity

Common Name	Fosetyl-aluminium
Function	Fungicide
Chemical Family	Phosphonate
Chemical Name	
1 **International Union of Pure and Applied Chemistry (IUPAC)**	aluminium tris(ethyl phosphonate)
2 **Chemical Abstracts Service (CAS)**	aluminum tris[ethyl phosphonate]
CAS Registry Number	39148-24-8
Molecular Formula	$C_6H_{18}AlO_9P_3$
Structural Formula	
Molecular Weight	354.10
Purity of the Technical Grade Active Ingredient	97% nominal (94.0-100%)
Registration Number	24563

2.2 Physical and Chemical Properties

Property	Result
Vapour pressure at 25°C	1×10^{-4} mPa
Ultraviolet (UV) / visible spectrum	λ_{max} in water = 223 nm (Not expected to absorb at $\lambda > 300$ nm)
Solubility in water at 20°C	111.3 g/L (pH 6)
n-Octanol/water partition coefficient	log K_{ow} = -2.1 to -2.7
Dissociation constant	pKa = 4.7

2.3 Registered Uses

Appendix I lists all fosetyl-Al products that are registered under the authority of the *Pest Control Products Act* as of 12 September 2017. One technical grade active ingredient product and six commercial class products are registered for use on greenhouse food and non-food crops, terrestrial food and feed crops, outdoor ornamentals and turf. Appendix II lists all the commercial class uses for which fosetyl-Al is presently registered.

3.0 Human Health Assessment

3.1 Toxicology Summary

Fosetyl-Al is an organophosphorous compound, but it has a structure and mode of action that is different from other organophosphate pesticides. A detailed review of the toxicological database for fosetyl-Al was conducted. The database consisted of the full array of toxicity studies currently required for hazard assessment purposes. The studies in the database were carried out in accordance with Good Laboratory Practices and international testing protocols that met the standards for testing at the time of their initial evaluation. The scientific quality of the data was acceptable and the database was considered complete to define the majority of the toxic effects that may result from exposure to fosetyl-Al.

Fosetyl-Al is comprised of aluminum and an organic portion, *O*-ethyl phosphonic acid. *O*-ethyl phosphonic acid is produced by dissociation of fosetyl-Al in the stomach of animals. Excess insoluble aluminum from fosetyl-Al is excreted predominantly via the feces in animals. Aluminum absorption in humans following an oral intake is small (0.2-1.5%), and the fractional absorption decreases with increasing dose in healthy humans (PMRA #2656770). Excretion of absorbed aluminum in humans occurs via kidneys; insoluble dietary aluminum is excreted primarily via feces.

Toxicokinetic investigations in animals assessed the *O*-ethyl phosphonic acid moiety alone as the parent compound. After gavage administration to rats, a single dose of radiolabeled *O*-ethyl phosphonic acid was rapidly and essentially completely absorbed and excreted. *O*-ethyl phosphonic acid was hydrolyzed to ethanol and phosphite, with ethanol subsequently oxidized

via acetaldehyde and acetate to CO_2. The highest radioactivity levels were found in the adrenal glands, gonads, spleen, kidneys, liver and brain, with the tissues and carcass retaining traces of the administered dose seven days after dosing. Elimination by all routes was slightly faster in female than male rats ($t_{1/2}$ of 184h and 129h, ♂/♀ respectively).

No *O*-ethyl phosphonic acid or its metabolites were detected in the lipid, protein or water soluble fractions of tissues. The longer half-life was representative of the incorporation of radiolabelled carbon, likely from acetate, into the metabolic pool of 2-carbon compounds, leading to the formation of normal cellular components. Twenty-four to 48 hours following single or multiple dosing, the primary route for excretion of radiolabelled carbon was expired air (as CO_2), followed by urine (as phosphonic acid, also called phosphorous acid) and feces. After administration of a single dose, the recovered urinary radioactivity was comprised mainly of the unchanged *O*-ethyl phosphonic acid, and after repeat dosing, the majority of the radioactivity recovered in the urine was phosphite, with the remainder as unchanged *O*-ethyl phosphonic acid. Administrated radiolabelled phosphite (metabolite) was excreted unchanged in both urine and feces, with only traces remaining in the body of orally dosed rats following repeated dosing.

Fosetyl-Al was of low acute oral toxicity in rats, mice, guinea pigs and rabbits, of slight acute toxicity via the inhalation route in rats and of low toxicity by the dermal route in rabbits. It was not a dermal sensitizer in guinea pigs or a dermal irritant in rabbits and caused mild eye irritation in rabbits. Clinical signs of acute oral toxicity included piloerection, sedation, and dyspnoea. Vomiting was noted in dogs only. However, since the actual treatment-dose in animals that vomited is unknown, the study was considered supplemental. Congestion of the digestive tract was observed in rodent and rabbit oral acute studies.

Two repeat-dose dermal toxicity studies, conducted with either rabbits or rats at or beyond a limit dose, identified local skin effects at the site of application but no systemic toxicity. In the rabbit, localized skin irritation was noted that included acanthosis and hyperkeratosis, while in the rat, skin damage, including increased erosion, hyperkeratosis, crusted areas and acute inflammation were observed.

The requirement for a repeat-dose inhalation study was waived based on a weight of evidence approach, taking into consideration the low vapour pressure of fosetyl-Al, low acute inhalation toxicity and the use pattern that is not expected to generate significant postapplication inhalation exposure.

In repeat-dose dietary studies in rats, the principal target organs of toxicity were kidney and urinary bladder. Other target organs were the spleen (90-day rat: extramedullary haematopoiesis) and male reproductive tract (two-year dog: testicular degeneration: seminiferous tubule degeneration and absence of spermatozoa). There were no other treatment-related effects in the 90-day or two-year dietary studies in dogs.

The changes in kidney and bladder were affected by duration of treatment and dose, with elevated urinary calcium and urinary phosphorous excretion in rats occurring as early as two weeks following initiation of treatment. Prolonged renal excretion of calcium and phosphorous caused the formation of calculi in the kidney and bladder. Fecal excretion of calcium was

unaffected by treatment, whereas fecal elimination of phosphorous was elevated in males with increased duration and dose.

In a 13-week dietary rat study with a 21-week recovery period, histopathological changes were observed in the kidneys (interstitial hydronephrosis and transitional cell hyperplasia) and bladder (calculi, papillary and transitional cell hyperplasia). Analysis of the urinary calculi showed high calcium and phosphorus content, and only minimal content of aluminum and magnesium. Higher incidences and increased size of calculi in the bladder and kidney occurred with increased duration of dosing. However, the incidence of bladder calculi decreased in the recovery period. There was a close correlation between incidence of calculi and proliferative lesions of the bladder mucosa.

The assessment of the oncogenic potential of fosetyl-Al included a battery of in vivo and in vitro genotoxicity studies, as well as long-term dietary studies in rats and mice. There was also a long-term rat dietary study and microbial point mutation studies for monosodium phosphite, the main urinary metabolite of fosetyl-Al.

In a chronic dietary rat study with fosetyl-Al, increased incidences of urinary bladder inflammation and tumors in the bladder and kidneys were observed. The incidence of bladder transitional cell papilloma and carcinoma, and combined incidence of papilloma and carcinoma were increased in high-dose males, a dose that exceeded the limit dose of testing. An increased incidence of kidney pelvis papillocarcinoma occurred in females beyond the limit dose. The effects on kidney and/or bladder, and formation of calculi in these organs, were not noted in either the dog study up to the limit dose, or in the long-term mouse study conducted with doses far exceeding the limit dose. Additionally, phosphite treatment did not cause calculi formation/ inflammation, or bladder or kidney tumors in a chronic dietary rat study.

A mode of action (MOA) for the bladder tumors was put forth by the registrant to explain the formation of urinary system tumors in rats. The MOA suggests that overloading with phosphorus and aluminum causes increased plasma calcium (Ca) and phosphorus (P). Increased Ca and P excretion via urine results in the formation of calculi/stone formation (urolithiasis) in the urinary system. The physical abrasion of the kidney and bladder by the calculi leads to inflammation, irritation and proliferation of the epithelium, followed by hyperplasia, and ultimately transitional cell papilloma and carcinoma. The induction of urinary bladder tumors by the irritating effect of foreign bodies such as calculi or implanted foreign material (for example, glass beads and paraffin wax pellets) has been reported in the published literature in support of this MOA (PMRA #2571837, 2571838, 2571839). Anatomical differences between rats and humans make rats more prone to induction of tumors by this MOA than humans. Even though clear evidence of calculi formation and progressive histopathological changes of the urinary system were noted in the 13-week oral rat study, which is consistent with the proposed MOA, the lack of a clear dose-response for calculi formation, inflammation and tumors in the chronic rat study was considered a limitation. A threshold approach to tumor development was deemed appropriate for risk assessment purposes, as there was no evidence of genotoxicity in the assays conducted with either fosetyl-Al or phosphite, and the evidence of oncogenicity was apparent only in rats and only above the limit dose of testing.

In the rat reproductive toxicity study, offspring effects were observed at a dose level that also resulted in maternal toxicity. Decreased body weights were noted for all generations (F_0, F_1 and F_2) on post-natal day (PND) 21 at the high-dose, at the mid-dose for the $F3_{a,b}$ generation on PND 12 and 21, and throughout most the post-natal period in the F3 high-dose group. Other offspring effects included increased renal pelvic dilatation at weaning, and increased urinary bladder epithelial hyperplasia in the high-dose group in $F3_b$ rats. Maternal toxicity manifested as decreased body weight gain during lactation, as well as urinary system effects. Histopathological changes were observed in the urinary tract of both adults and offspring in the high-dose groups. Although fosetyl-Al did not affect reproductive parameters, this reproductive toxicity study was older and did not capture endpoints measured in current reproductive toxicity studies (such as total cauda epididymal sperm number, percent progressively motile sperm, percent morphologically normal sperm, and percent of sperm with abnormalities). The lack of these measures raises some uncertainty with respect to potential effects on fertility, given the testicular effects noted in the two-year dog study (seminiferous tubule degeneration).

No malformations occurred below the limit dose of testing in gavage developmental toxicity studies in rats and rabbits. In a developmental toxicity study in rats, treatment-related effects occurred only at doses well in excess of the limit dose. Fetal effects included decreased body weights, skeletal and visceral malformations (thoracic asymmetry, kidney displacement, renal pelvic cavitation, vein/artery transposition, displaced testes, abdominal and subcutaneous cranial haemorrhage, hydrocephaly (considered equivocal)) and delayed ossification. An increased incidence of total resorptions was noted, with concomitant decrease in average litter size, in the high-dose rats. At the same dose, significant maternal toxicity occurred as evidenced by mortality, clinical signs of toxicity and decreased body weight gain.

In a rabbit developmental toxicity study, the only fetal effect was an increased incidence of distended ureter observed at a dose causing no maternal toxicity. No treatment-related malformations were observed in rabbits. In a co-critical range-finding developmental toxicity study in rabbits, increased post-implantation loss, and decreased mean number of live fetuses were noted at doses higher than in the definitive study (above). These findings occurred in the presence of maternal toxicity (body weight and body-weight gain reduction, mortality). In both the supplemental developmental toxicity study in rabbits and the supplemental range-finding developmental toxicity study in rabbits, there were no treatment-related developmental effects noted at doses that were higher than those in the definitive study.

Although no specific neurotoxicity studies were submitted, there was no evidence suggestive of neurotoxicity following acute, short-term or chronic dosing in multiple species in the fosetyl-Al database at dose levels greater than the limit dose. Therefore, the concern for neurotoxicity for fosetyl-Al is low.

Results of the toxicology studies conducted on laboratory animals with fosetyl-Al are summarized in Appendix III, Table 1. The toxicology endpoints for use in the human health risk assessment are summarized in Appendix III, Table 2.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Product Act* requires the application of an additional 10-fold factor to threshold effects to take into account the completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to completeness of the toxicity database as it pertains to the toxicity to infants and children, the fosetyl-Al database contains the standard complement of required studies, including developmental toxicity studies in rats and rabbits, and a multi-generational reproductive toxicity study in rats. There was no concern for potential developmental neurotoxicity as there was no evidence of neurotoxicity in the database.

In accordance with the *Pest Control Products Act*, the protection and consideration afforded to children also extends to future generations. In a two-year oral dog study, seminiferous tubule degeneration with potential effects on fertility was observed. The level of concern for the potential impact on ability to produce future generations is tempered by the fact that the endpoint selection for risk assessment provides adequate margins of exposure for this effect.

In the oral rat reproductive toxicity study, offspring effects including decreased body weight, increased renal pelvic dilation (at weaning) and increased urinary bladder epithelial hyperplasia, were observed at a dose level that also resulted in maternal toxicity. Maternal toxicity manifested as decreased body weight gain during lactation and urinary system changes.

In a rat developmental toxicity study, treatment-related effects occurred only at doses well in excess of the limit dose of testing, and with concurrent significant maternal toxicity. Fetal effects included decreased body weights, skeletal and visceral malformations (thoracic asymmetry, kidney displacement, renal pelvic cavitation, vein/artery transposition, displaced testes, abdominal and subcutaneous cranial haemorrhage, hydrocephaly) and delayed ossification. The incidence of total resorptions at the high-dose was also increased, with concomitant decrease in average litter size. In a rabbit developmental toxicity study, distended ureter was observed at a dose causing no maternal toxicity, indicating sensitivity of the young; however the effect was not of a serious nature. Furthermore, there were no adverse effects noted in the supplementary developmental toxicity study, and no malformations in the range finding developmental toxicity study, which used higher doses.

Overall, the database is adequate for determining the sensitivity of the young, and effects on the young are well-characterized. The selection of endpoints for risk assessment provides protection for the testicular effects noted in the dog, as well as the effects noted in the developing fetus. Consequently, the *Pest Control Products Act* factor is reduced to 1-fold.

3.2 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide, including residues in meat and milk, may be ingested with the daily diet. Exposure to fosetyl-Al from potentially treated imported foods is also included in the assessment. Dietary exposure assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when exposure exceeds 100% of the reference dose. The PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessment procedures.

Sufficient information was available to adequately assess the dietary risk from exposure to fosetyl-Al. Chronic dietary exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™, Version 4.02) program which incorporates consumption data from the National Health and Nutrition Examination Survey, What We Eat in America (NHANES/ WWEIA) 2005-2010 available through the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics (NCHS). Further details on the consumption data are available in Science Policy Note SPN 2014-01, *General Exposure Factor Inputs for Dietary, Occupational and Residential Exposure Assessments*.

3.2.1 Determination of Acute Reference Dose

There were no effects in the database warranting the establishment of an acute reference dose for fosetyl-Al.

3.2.2 Acute Dietary Exposure and Risk Assessment

An acute dietary exposure and risk assessment was not required.

3.2.3 Determination of Acceptable Daily Intake (ADI)

General Population (including pregnant women, infants and children)

To estimate risk from repeated dietary exposure, a no observed adverse effect level (NOAEL) of 88 mg/kg bw/day from the two-year dietary study in rats was selected for risk assessment, based on the increased incidence of urinary bladder inflammation in male rats at a lowest observed adverse effect level (LOAEL) of 348 mg/kg bw/day.

Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As noted in the *Pest Control Products Act* Hazard Characterization section above, the *Pest Control Products Act* factor was reduced to 1-fold. Therefore, the composite assessment factor (CAF) is 100.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{88 \text{ mg/kg bw/day}}{100} = 0.9 \text{ mg/kg bw/day of fosetyl-Al}$$

This ADI provides a margin of 343 to the NOAEL of 309 mg/kg bw/day for testicular effects in the dog, >1500 to the dose causing bladder and kidney tumors in rats, 1111 to the NOAEL of 1000 mg/kg bw/day for developmental toxicity noted in the rat developmental toxicity, and 111 to NOAEL of 100 for rabbit developmental toxicity.

3.2.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated using the average consumption of different foods and drinking water, and the average residue values on those foods and in drinking water. The ADI is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects. The estimated exposure was then compared to the ADI. When the estimated exposure is less than the ADI, the chronic dietary exposure is not of concern.

Fosetyl-Al is metabolized to phosphonic acid (also called phosphorous acid) in foods and in drinking water. Due to the potential concentration of this metabolite in food and drinking water, and due to its potential toxicity (assumed to have the same toxic potential as fosetyl-Al), the dietary exposure assessment considered exposures to both the parent compound and the metabolite.

Residue estimates for dietary exposure may be based on maximum residue limits (MRLs), both Canadian and international, or anticipated residues from field trial data. These estimates are considered to be conservative (resulting in upper-bound or high-end estimates), since they represent residues at the highest maximum label rate measured in the field. In the case of fosetyl-Al, Canadian MRLs and United States Environmental Protection Agency (USEPA) tolerances are specified for the parent only. Field trial data available to the PMRA measure mainly for fosetyl-Al and there are limited data for phosphonic acid. Therefore, these MRLs/tolerances or data could not be used for the dietary risk assessment, as they do not capture potential residues of phosphonic acid. Surveillance data from the Canadian Food Inspection Agency or the United States Department of Agriculture Pesticide Data Program did not measure fosetyl-Al or phosphonic acid. However, the European Union (EU) has established MRLs for both the parent compound and the metabolite based on field trials conducted in European countries. Some of the field trials were conducted under conditions that were comparable to the Canadian use pattern. Therefore, for the dietary risk assessment of fosetyl-Al, EU MRLs or the residues from EU field trial data were used when acceptable Canadian field trial data were not available. As MRLs and field trial data result in high-end estimates of exposure, it is not expected that exposure to fosetyl-Al and phosphonic acid will be underestimated in the risk assessment. Other inputs for the dietary risk assessment included percent crop treated data and domestic production and import statistics, available experimental processing factors or default DEEM processing factors,

and the chronic drinking water estimated environmental concentration (EEC) point estimate obtained from modelling (see Section 3.3). For more information on dietary risk estimates and the residue chemistry information used in the dietary assessment, see Appendices IV and V.

The chronic dietary exposure estimates (from food and drinking water) ranged from 13-49% of the ADI, with the highest exposed subpopulation being children aged 1 to 2 years. These chronic dietary exposures to fosetyl-Al and its metabolite, phosphonic acid, do not pose dietary risks of concern.

3.2.5 Cancer Assessment

Fosetyl-Al is not likely to pose a tumorigenic hazard in humans, based on an assessment of the weight of evidence. Fosetyl-Al produced bladder tumors in male rats (predominantly) and kidney tumors in female rats by a non-genotoxic mode of action and only at extremely high-doses (exceeding the limit dose). It was not carcinogenic in mice and was not considered mutagenic in a battery of genotoxicity assays. The urinary metabolite of fosetyl-Al, monosodium phosphite, did not produce a carcinogenic response in rats and was also non genotoxic. Although the registrant-proposed MOA for the formation of urinary system tumors in rats was not completely supported by the data, there was sufficient information to support a threshold approach. The current dietary reference dose (ADI) and the selected margins of exposure (MOEs) for occupational and bystander exposures provide an adequate margin of >1500 to the dose causing bladder and kidney tumors in rats.

3.2.6 Cancer Dietary Exposure and Risk Assessment

A separate quantitative cancer assessment was not required (See Section 3.2.5).

3.3 Exposure from Drinking Water

Residues of fosetyl-Al in potential drinking water sources were estimated from modelling.

3.3.1 Concentrations in Drinking Water

Estimated Concentrations in Drinking Water Sources

EECs of fosetyl-Al in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of fosetyl-Al in groundwater were calculated using the PRZM-GW model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZM-GW are average concentrations in the top 1 m of the water table.

EECs of fosetyl-Al in surface water were calculated using the Surface Water Concentration Calculator model, which simulates pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir.

A drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The EEC estimates are expected to allow for future use expansion into other crops at this application rate. Appendix IX, Table 1 lists the main environmental fate characteristics used in the simulations. Initial application dates between March and October were modelled and the reported values are from the run yielding the maximum EEC. The model was run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Appendix IX, Table 3.

Water Monitoring Data

A search for monitoring data on fosetyl-Al in Canadian waterbodies was conducted. Databases from the United States were also searched for fosetyl-Al water monitoring data. Data on residues present in water samples taken in the United States are important to consider in the Canadian water assessment given the extensive monitoring programs that exist in the United States. Local weather patterns, runoff events, circumstantial hydrogeology, and testing and reporting methods are probably more important influences on residue data than Northern versus Southern climate. As for climate, if temperatures are cooler, residues may break down more slowly; on the other hand if temperatures are warmer, growing seasons may be longer and pesticide inputs may be more numerous and frequent.

The following large American databases were searched for monitoring data: the United States Geological Survey's National Water Quality Assessment Program, the USEPA Storage and Retrieval Data Warehouse, and the California Department of Pesticide Regulation's Surface Water Protection Program database. Annual Reports from the United States Department of Agriculture's Pesticide Data Program were also included in the search.

No Canadian or American monitoring data were available for fosetyl-Al in water. Due to the lack of monitoring data, an estimation of the residues of fosetyl-Al in waterbodies relevant for aquatic risk assessment purposes, or in drinking water sources for Canadians using monitoring data is not possible. The EECs for ecoscenario and drinking water sources determined through water modelling were used in the risk assessments for aquatic organisms and human health, respectively.

3.3.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were combined with food exposure estimates, with EEC point estimates incorporated directly in the dietary (food and drinking water) assessments. Please refer to Sections 3.2.2 and 3.2.4 for details.

3.4 Occupational and Non-Occupational Exposure and Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean

that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.4.1 Toxicology Endpoint Selection for Occupational and Non-Occupational Risk Assessment

Dermal and Inhalation Exposure

For short-and intermediate-term dermal and inhalation risk assessments, for all populations, a NOAEL of 100 mg/kg bw/day was selected based on fetal effects in the oral developmental toxicity study in rabbit. An increased incidence of distended ureter was noted in fetuses at the LOAEL of 300 mg/kg bw/day. The target MOE is 100 and includes uncertainty factors of 10-fold for interspecies extrapolation, and 10-fold for intraspecies variability. This is considered protective of all populations, including nursing infants and the unborn children of exposed female workers.

For long-term dermal and inhalation risk assessments, for all populations, a NOAEL of 88 mg/kg bw/day for males in the two-year dietary rat study was selected based on increased bladder inflammation at LOAEL of 348 mg/kg bw/day. The target MOE is 100 and includes uncertainty factors of 10-fold for interspecies extrapolation, and 10-fold for intraspecies variability. This is considered protective of all populations, including nursing infants and the unborn children of exposed female workers.

Dermal Absorption

An adequate dermal absorption study was not available for fosetyl-Al. The dermal absorption factor was reduced from the default of 100% to 50% based on a weight-of-evidence approach using available dermal absorption studies (a limited rat and human in vitro study), the physical/chemical properties of fosetyl-Al and its metabolites, and observations from toxicology studies.

3.4.2 Non-Occupational Exposure and Risk Assessment

The non-occupational (residential) risk assessment involves estimating risks to the general population, including youth and children, during or after pesticide application.

Residential Applicator Exposure and Risk Assessment

A residential applicator refers to an adult who uses or applies a domestic-class product in or around the home. Domestic-class products containing fosetyl-Al are not registered in Canada. Therefore, a residential applicator assessment is not required.

Residential Postapplication Exposure and Risk Assessment

Residential postapplication occurs when an individual is exposed through dermal, inhalation, and/or incidental oral (non-dietary ingestion) routes as a result of being in a residential environment that has been previously treated with a pesticide or handling treated plants during gardening. For fosetyl-Al, postapplication exposure may occur while gardening with bedding plants or entering treated golf courses. No data were submitted to assess postapplication residential exposure.

The USEPA has generated standard default assumptions for developing residential exposure assessments for postapplication exposures when chemical- and/or site-specific field data are limited. The assumptions and algorithms may be used in the absence of, or as a supplement to, chemical- and/or site-specific data and generally result in high-end estimates of exposure. The assumptions and algorithms relevant to the fosetyl-Al re-evaluation are outlined in the Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessments 2012 under "Section 3: Lawns and Turf" and "Section 4: Gardens and Trees".

There is potential for short-term dermal exposure to adults, youth (11 to <16 years old), and children (6 to <11 years old) through contact with transferable residues following application of fosetyl-Al. Inhalation exposure to outdoor applications was considered to be minimal due to the low vapour pressure of fosetyl-Al and the expected dilution in outdoor air.

Calculated MOEs for dermal residential postapplication exposure to fosetyl-Al exceeded the target MOE and are not of concern. The residential postapplication risk assessment is outlined in Appendix VI, Tables 1 and 2. Since products containing fosetyl-Al are only to be used in golf courses, a label statement is proposed to clarify that products cannot be used on other residential turf including lawns, gardens, playing fields, cemeteries, and schools.

3.4.3 Occupational Exposure and Risk Assessment

Workers can be exposed to fosetyl-Al through mixing, loading, or applying the pesticide, and when entering a previously treated site to conduct activities.

Handler Exposure and Risk Assessment

There are potential exposures to mixers, loaders and applicators. The following scenarios were assessed:

- Mixing/loading of dry flowables (used as a surrogate for wettable granules);
- Mixing/loading of wettable powders;
- Applying liquids by groundboom to blackberries, red/black raspberries, brassica leafy vegetables, ginseng, lettuce, onions, spinach, cranberries, rutabaga, strawberries, tobacco, and turf;

- Applying liquids by airblast to apples (bearing and non-bearing), blackberries, red/black raspberries, highbush blueberries, grapes (including table grapes), ornamental plants (field grown in nurseries and landscape plantings) and conifers grown in nurseries and landscape plantation;
- Mixing/loading of dry flowable and wettable powders to be applied by chemigation to cranberries;
- Applying liquids by turf gun to turf (golf courses, sod farms, and turf areas);
- Applying liquids by manually pressurized hand wand and backpack to apples (bearing and non-bearing), Belgian endives, blackberries, red/black raspberries, brassica leafy vegetables, highbush blueberries, lettuce, onions, spinach, cranberries, strawberries, tobacco, bedding plants, ornamental plants, turf, greenhouse broccoli and cabbage transplants, greenhouse lettuce, and greenhouse ornamentals; and
- Applying liquids by mechanically pressurized hand gun to apples (drench application), blackberries, red/black raspberries, highbush blueberries, strawberries, tobacco, bedding plants (drench), ornamental plants, greenhouse broccoli and cabbage transplants (drench), greenhouse lettuce, and greenhouse ornamentals.

Based on the number of applications and the timing of application, workers applying fosetyl-Al would generally have a short-term exposure (<30 days) to the pesticide. Exposure to mixers/loaders and applicators was assumed to be to the parent compound only. It was assumed that the metabolite, phosphonic acid, would not be formed in significant quantities when the product has not been exposed to the outside environment.

Handler exposure was estimated based on different levels of personal protective equipment (PPE):

- Baseline PPE: long pants, long-sleeved shirts and chemical-resistant gloves (unless otherwise specified). For groundboom application, this scenario does not include gloves, as the data quality was better for non-gloved scenarios than gloved scenarios.
- Mid-Level PPE: cotton coveralls over long pants, long-sleeved shirts and chemical-resistant gloves.
- Max-Level PPE: chemical-resistant coveralls over long pants, long-sleeved shirts and chemical-resistant gloves.
- Chemical-resistant headgear: Chemical-resistant headgear that covers the neck (for example, Sou'Wester hat, rain hat).

No appropriate chemical-specific handler exposure data were available for fosetyl-Al. Therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), Version 1.1, and studies from the Agricultural Handler Exposure Task Force (AHETF) and Outdoor Residential Exposure Task Force (ORETF). The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE. In most cases, these studies did not contain appropriate data sets to estimate exposure to workers wearing coveralls.

This was estimated by incorporating a 75% clothing protection factor for coveralls, where applicable. Inhalation exposures were based on light inhalation rates (17 L/min) except for backpack applicator scenarios, which were based on moderate inhalation rates (27 L/min).

Calculated dermal, inhalation, and combined (total exposure from dermal and inhalation routes) MOEs for mixer/loaders and applicators with mid-level and/or max-level PPE exceeded the target MOE of 100 for all scenarios and are not of concern, with the exception of the groundboom application of wettable powder product(s) to turf, and the mechanically pressurized hand gun application to blackberries, red/black raspberries, and strawberries, even with the max-level PPE applied (Appendix VII, Table 1). To mitigate the potential risk resulting from the use on turf, it is proposed to limit the amount handled per day to 320 kg a.i./day for wettable powder product(s). To mitigate the potential risk resulting from the use on these berries, it is proposed to change the label spray volume of application from 200-1000 L/ha to 250-1000 L/ha (wettable granule) and 300 -1000 L/ha (wettable powder), in addition to the requirement of chemical-resistant coveralls. There are no data available to assess commercial application using fogging equipment (handheld or automated) or handheld mistblowers. It is proposed to prohibit these types of application equipment. The proposed label amendments are specified in Appendix X.

Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considers exposures to workers who enter previously treated sites to conduct agronomic activities involving foliar contact (such as scouting). Based on the use pattern for fosetyl-Al, there is potential for short- to intermediate-term exposure for outdoor workers, and long-term exposures for greenhouse workers.

Potential exposure to postapplication workers was estimated using updated activity-specific transfer coefficients (TCs), and chemical-specific dislodgeable foliar residue (DFR)/turf transferable residue (TTR), if available. The DFR/TTR refers to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant or the surface of a lawn. The TC is a measure of the relationship between exposure and DFR/TTR for individuals engaged in a specific activity, and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination (for example, thinning apples) and reflect standard agricultural work clothing worn by adult workers. Activity-specific TCs from the Agricultural Re-Entry Task Force (ARTF) were used. Postapplication exposure activities for agricultural crops include (but are not limited to): harvesting, thinning, pruning and scouting. For more information about estimating worker postapplication exposure, refer to the PMRA's Regulatory Proposal PRO2014-02, *Updated Agricultural Transfer Coefficients for Assessing Occupational Postapplication Exposure to Pesticides*.

There were no chemical specific DFR or TTR studies submitted to the PMRA for the re-evaluation of fosetyl-Al; therefore, the following defaults were used:

- A default peak DFR value of 25% of the application rate with a dissipation rate of 10% per day was used for outdoor crops.

- A default peak DFR value of 25% of the application rate with a dissipation rate of 0% per day was used for greenhouse food crops.
- A default peak DFR value of 25% of the application rate with a dissipation rate of 2.3% per day was used for greenhouse ornamentals.
- A default peak TTR value of 1% of the application rate with a dissipation rate of 10% per day was used for turf.

The PMRA's Science Policy Note SPN2014-02, *Estimating Dislodgeable Foliar Residues and Turf Transferable Residues in Occupational and Residential Postapplication Assessments* presents further details on the derivation and use of these defaults for pesticide assessments.

No data were available to estimate potential postapplication worker exposure to the metabolite, phosphonic acid. However, due to conservative inputs used in the exposure assessment, potential risk from phosphonic acid is not expected to be underestimated.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application to perform tasks involving hand labour. An REI is the duration of time that must elapse in order for residues to decline to a level at which there are no risks of concern for postapplication worker activities (for example, in the case of fosetyl-Al, performance of a specific activity that results in exposures above the target MOE of 100).

The PMRA is primarily concerned with the potential for dermal exposure for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of fosetyl-Al, inhalation exposure is not likely to be of concern provided that the minimum 12-hour REI is followed.

For most field crops, calculated dermal MOEs for worker postapplication exposure to fosetyl-Al exceeded target MOEs at the REIs specified on the current labels or at an REI of 12 hours, and risks are not of concern (Appendix VIII, Tables 1-4). Longer REIs are proposed for some crops for which target MOEs were not met (apples, blackberries, red/black raspberries, highbush blueberries, grapes, brassica leafy vegetables, onions, spinach and ornamental plants). For additional information, refer to Appendix X for the proposed label amendments. Stakeholders are encouraged to provide comments on the feasibility of these proposed REIs or to propose other possible mitigation measures (for example, lower application rates), during the consultation period.

For greenhouse crops, calculated dermal MOEs exceeded target MOEs at the REIs specified on the current labels or at an REI of 12 hours, for all activities with the exception of activities for bedding plants and cut flowers, which are discussed further below (Appendix VIII, Tables 1-4).

For Belgian endive, a quantitative exposure assessment was not conducted, since it was determined that the potential for worker exposure is very low. Fosetyl-Al is applied to harvested roots for chicon production only. Postapplication exposure is considered to be very low due to the lack of activities in the forcing room where the workers may be handling the treated

beddings. A pre-harvest interval (PHI) of 21 days is specified on the current labels. Limited soil/root surface contact is expected to occur at harvest, which is done by hand or mechanically.

Fosetyl-Al is registered for use as drench application to greenhouse broccoli and cabbage transplants (1.6-2.4 kg a.i./ha). Worker exposure was estimated for both foliar contact and soil contact. To estimate exposure from contact with treated soil during transplanting, the dermal exposure equation for soil contact from the USEPA Risk Assessment Guidance for Superfund was used (USEPA, 2004).The calculated MOE for soil-contact exposure was greater than the target MOE (Appendix VIII, Table 4). For foliar contact, a standard postapplication exposure assessment using TC values was conducted. Target MOEs for foliar contact were met for greenhouse broccoli and cabbage transplants (Appendix VIII, Table 1). Therefore, worker risks are not of concern at the minimum REI of 12 hours.

For greenhouse/outdoor bedding plants, similar assessments as those for greenhouse broccoli and cabbage transplants were conducted. Two types of application methods for bedding plants are specified on the labels: drench application and foliar application, with the latter assumed to be spray applications. The calculated MOE for soil-contact exposure was greater than the target MOE (Appendix VIII, Table 4) for both application methods. For foliar contact following spray application (2.24 kg a.i./ha), the calculated MOE was greater than the target MOE. However, for drench application (80 kg a.i./ha), the calculated MOE was below the target MOEs on the day of application; to reach the target MOE, an REI of 28 days (outdoor) or 60 days (greenhouse) would be required, which is not agronomically feasible (Appendix VIII, Table 1). Therefore, the drench application to bedding plants is proposed for cancellation. It should be noted that bedding plants have a high drench application rate compared to the spray application rate. Further use pattern information for the drench application on bedding plants is sought during the consultation period. In addition, alternative mitigation measures such as reducing the application rate or specifying the application equipment (for example, direct soil drench with no foliar contact), may be further explored if support is provided as part of stakeholder feedback during the consultation period.

For greenhouse/outdoor cut flowers, an REI of 9 days (outdoor) or 71 days (greenhouse) would be required to reach the target MOE (Appendix VIII, Table 2). This REI is not agronomically feasible, and therefore, this use is proposed for cancellation. The PMRA is seeking further use pattern information during the consultation period for this use such as:

- What types of cut flowers receive fosetyl-Al applications and what activities occur for these flowers? The current labels specify all ornamentals in general, which limits potential mitigation options.
- Is foliar application required for cut flowers? Could applications occur in soil, which would greatly reduce potential worker exposure from contact with foliage?

The postapplication exposure assessment is outlined in Appendix VIII, Tables 1-4. For guidance on REIs, please refer to the *Guidance for Federal/Provincial/Territorial Committee: Understanding Restricted-Entry Intervals for Pesticides*, which is available from the PMRA upon request.

3.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Risk estimates were performed for those scenarios when the individual exposure routes met the target MOEs and were not of concern.

3.5.1 Toxicology Endpoint Selection for Aggregate Risk Assessment

Short-term Aggregate

Short-term aggregate exposure to fosetyl-Al may be comprised of food, drinking water and residential exposures. The most relevant study is the oral developmental rabbit toxicity study with a NOAEL of 100 mg/kg bw/day, based on fetal effects, which were non-serious in nature, in the absence of maternal toxicity. This is the lowest relevant NOAEL in the database, and effects are relevant to all routes of exposure. The target MOE is 100, based on factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization Section.

3.5.2 Residential, Non-Occupational and Dietary Aggregate Exposure and Risk Assessment

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated. Scenarios where a quantitative risk assessment was conducted and which did not have risks of concern were aggregated to determine whether aggregation of exposures would result in risks of concern.

For fosetyl-Al, the following scenario is expected to co-occur:

- Postapplication dermal exposure (adults, youth and children (6 to <11 years old)) from activities on treated golf courses + chronic dietary (food and drinking water).
- Postapplication dermal exposure (adults, youth and children (6 to <11 years old) from gardening activities with bedding plants + chronic dietary (food and drinking water).

All calculated MOEs exceeded the target MOE and are not of concern. The aggregate exposure estimates from residential scenarios are presented in Appendix VI, Table 3.

3.6 Cumulative Assessment

The *Pest Control Products Act* requires the Agency to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Fosetyl-Al belongs to a group of fungicides producing phosphonic acid. Other currently registered phosphonic acid-releasing fungicides are mono- and di-potassium salts of phosphorous acid, and mono- and dibasic

sodium, potassium, and ammonium phosphites. A cumulative dietary exposure from use of all phosphonic acid-producing pesticides will be conducted in the future when toxicological endpoints and food residue data for phosphonic acid become available.

3.7 Incident Reports – Human Health

As of 10 July 2017, the PMRA had received three incidents reports involving fosetyl-Al. The incidents were classified as major or minor in severity. The major incident involved an individual and her dog, who reported being exposed to several active ingredients including fosetyl-Al after application to a ginseng farm. Reported symptoms included irritated eyes or seizure. Details relating to fosetyl-Al exposure were not provided in the report and hence there was insufficient information to evaluate the incident. The two minor incidents were considered to be related to the reported pesticide exposure. Individuals experienced symptoms like itchy skin, red skin, rash or lesion either as a result of contact with a fosetyl-Al product following equipment failure or by inhaling fumes created while soldering a pipe.

A search of the California Pesticide Illness Database (1992 to 2011) revealed 101 human incidents involving fosetyl-Al. In most reports, fosetyl-Al exposure was reported in conjunction with other active ingredients. All cases, with the exception of one, occurred in an agricultural setting, and the application site frequently cited in these incidents related to lettuce (64%). Overall, the commonly reported symptoms in the database include effects such as dizziness, headache, skin and eye irritation.

The USEPA reviewed incident data involving the product Aliette (containing fosetyl-Al) from three databases: the USEPA Incident Data System (1999 to 2007), the American Poison Control Center (1993 to 2005) and the Centers for Disease Control and Prevention/National Institute for Occupation Safety Sentinel Event Notification System for Occupational Risk-Pesticides (1998 to 2003). Across all examined databases, the relative numbers of human incidents involving Aliette were of low severity and frequency. Effects associated with skin and ocular irritation were commonly reported. The USEPA recommended no mitigation actions as being necessary at the time of the review (2007).

Since no serious health concerns were identified from the incident data and current labels indicate "avoid contact with skin" or "harmful in contact with skin", no additional changes to labels are proposed.

4.0 Environmental Assessment

4.1 Fate and Behaviour in the Environment

Information on the fate and behaviour of fosetyl-Al and its major transformation products are summarized in Appendix IX, Tables 1 and 2.

Abiotic Transformation

Fosetyl-Al is very soluble in water (110 g/L at 20°C) and not likely to bioaccumulate (log K_{ow} = -2.1). Based on vapour pressure, fosetyl-Al is classified as having low volatility (vp < 1×10^{-7} Pa) and is non-volatile from water and moist soil surfaces (Henry's Law Constant = 3.1×10^{-15} atm. m^3mol^{-1} (calculated)).

Fosetyl-Al is stable to hydrolysis at naturally occurring pHs tested. Photolysis is not expected in the environment as the active ingredient does not absorb light at environmentally relevant wavelengths. The vapour pressure and Henry's Law constant indicate that fosetyl-Al will not volatilize from water or soil surfaces.

Biotransformation in Soil

Fosetyl-Al transforms rapidly in aerobic soil, having a DT_{50} (dissipation time to 50%) of < 1 day. The major transformation products are ethanol and phosphonic acid. Ethanol is degraded rapidly in soil, while phosphonic acid is moderately persistent. The DT_{50} for phosphorous acid is up to 157 days. In anaerobic soil, the DT_{50} for fosetyl-Al is up to 2 days (12-50 hours). These results indicate that fosetyl-Al and the major transformation product, ethanol (DT_{50} of 12-15 hours), are expected to be non-persistent in soil under anaerobic conditions.

Aquatic Biotransformation

Fosetyl-Al transforms rapidly in aerobic aquatic environments. The DT_{50} in water sediment systems was determined to be 3.9-4.5 days for the whole system. The parent chemical dissipates rapidly by mineralization and does not partition to sediment. The major metabolite is ethanol, and is associated with the water phase. Phosphonic acid is expected to be released into water based on soil studies, however, due to the rapid adsorption to sediment, it is assumed to be unavailable in water. Furthermore, the anaerobic aquatic study determined that phosphorous acid is not likely to be formed in aquatic systems.

Mobility

Fosetyl-Al does not adsorb to soils and would be classified as mobile based on adsorption studies in three soils. However, the parent chemical is rapidly transformed in soil and is not expected to be mobile under field conditions. The transformation product ethanol is mobile and volatile, while phosphonic acid is adsorbed to soil and is slightly mobile. Fosetyl-Al satisfies some of the criteria for leaching, however, based on the very short half-life of the active ingredient in soil and the results of water modelling, it is not expected to leach in soil or enter groundwater. Fosetyl-Al is non-volatile and is not expected to be subject to long range transport.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects

occur. Estimated environmental concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rates, chemical properties and environmental fate properties, including the dissipation of the pesticide between applications (Appendix IX, Tables 3-7). Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (protection at the community, population, or individual level) (Appendix IX, Tables 8-10).

The EECs and the risk to the environment were determined using the application rate for spinach (7 × 3.6 kg a.i./ha) and turf (4 × 9.6 kg a.i./ha), being the highest crop and non-crop use rates. Additionally, some other use rates were also characterized as appropriate, for example application on lettuce to determine risk to mammals and application in apple orchards to determine risk from spray drift.

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the RQ is then compared to the level of concern (LOC = 1, except for *Typhlodromus pyri* and *Aphidius* screening level studies which have an LOC = 2, and bees, which have an LOC = 0.4). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

Terrestrial Invertebrates

See Appendix IX, Tables 11-12 for details on the toxicity, exposure and risk to terrestrial invertebrates.

Earthworms

The RQs for earthworms were determined using the 14-day LC_{50} (median lethal concentration) > 746-1000 mg a.i./kg soil value with a 2× safety factor for the earthworm *Lumbricus terrestris* (14-day LC_{50} >373 mg a.i./kg soil). The LOC is not exceeded.

Bees – Contact Exposure

Toxicity: The acute contact LD_{50} of > 1000 µg a.i./bee was used to determine risk from exposure to the active ingredient. For the tested product, the LD_{50} of > 312 µg a.i./bee was used. For the soil transformation product phosphonic acid (H_3PO_3), the acute contact LD_{50} of > 29.7 µg/bee was used.

Exposure concentration: The EEC was determined for the two highest use rates of fosetyl-Al, spinach and turf (sod), which are not attractive crops to bees. In order to compare the application rate to the toxicity endpoints derived in laboratory studies (µg a.i./bee), a conversion from kg a.i./ha to µg a.i./bee is required. The proposed upper-bound residue value for estimating exposure to bees is based on the maximum residue value reported by Koch and Weißer (1997).

The EEC for the active ingredient (for spinach and turf) is 3.6-9.6 kg a.i./ha × 2.4 µg a.i./bee per kg/ha = 8.6-23 µg a.i./bee for the above two use rates, respectively. The EEC for phosphonic acid is 1.99-5.3 µg /bee, (assuming 100% conversion and a 23.1% residual rate based on the molar mass).

Risk: When compared to the acute contact endpoint of > 1000 µg a.i./bee, the LOC (0.4) is not exceeded for either of the two use rates (RQ < 0.023). Similarly, the RQ for the tested product is expected to be < 0.07. The acute contact RQ for the transformation product phosphonic acid is < 0.18.

Bees – Oral Exposure

Toxicity: The acute oral toxicity LD_{50} value of 462 µg a.i./bee was used to determine risk for the active ingredient. For the tested product, the toxicity value used was LD_{50} >352 µg a.i./bee. For the transformation product phosphonic acid, the acute oral LD_{50} > 212 µg/bee was used.

Exposure concentration: Initially, the EEC was determined for the two highest use rates of fosetyl-Al, spinach and turf (sod), which are not attractive crops to bees. In addition, the rate for bee attractive crops such as blueberries and strawberries was also considered, since they represent attractive crops for bees. The oral exposure estimate for adult bees is calculated by multiplying the direct single rate by 29 µg a.i./bee per kg/ha. This conversion is based on consumption rates primarily derived from Rortais et al. (2005) and Crailsheim et al. (1992 and 1993).

The EEC for the active ingredient (for spinach and turf) is 3.6-9.6 kg a.i./ha × 29 µg a.i./bee per kg/ha = 104.4-278.4 µg a.i./bee, respectively. The EEC for blueberries and strawberries is 4.48 kg a.i./ha × 29 µg a.i./bee per kg/ha = 130 µg a.i./bee. The EEC for phosphonic acid is 24.1-64.3 µg /bee (assuming 100% conversion and a 23.1% residual rate based on the molar mass).

Risk: When compared to the acute oral endpoint of 462 µg a.i./bee, the LOC (0.4) is not exceeded for the high use rate on crops such as spinach (RQ = 0.23), but is exceeded based on a

single application to turf (RQ = 0.6). The RQ for the tested product is < 0.3 for spinach, which is below the LOC of 0.4, and is therefore not expected to pose a risk. However, the RQ of the tested product for turf is 0.79, which exceeds the LOC. Although the LOC is slightly exceeded for turf use only, turf (sod) is not attractive to bees and as such, application to turf is not expected to result in exposure for pollinators. If we further consider potential exposure to bee attractive crops such as blueberries and strawberries, the LOC is not exceeded (RQ = 0.28).

The RQ for acute oral exposure to the transformation product phosphonic acid is < 0.11 for spinach and < 0.3 for turf.

Although no larval or chronic adult bee studies were available for review, the potential chronic risk to these castes of bees could be evaluated from the semi-field study.

Semi-field study: A semi-field study with bees is available with an end-use product containing 80% fosetyl-Al applied at 80 kg product/ha. The effect of this product was examined on small bee colonies in cages placed over field plots with flowering *Phacelia tanacetifolia*. The product was applied before sowing of the *Phacelia* and then once more at approximately 30% flowering. The bees were introduced 28 hours after the last application. In this study no effects on bee mortality, bee brood development or behavior of the bees was observed.

Assumptions and uncertainties:

- The second application is assumed to have been a foliar application.
- The reported application rate of 80 kg product/ha (64 kg a.i./ha) is assumed to be the cumulative rate based on two applications, which means that each application was of 32 kg a.i./ha.
- The exposure of bees to the active ingredient and its transformation product phosphonic acid may have occurred from the second application only, because the first application was made to soil pre-seeding and the active ingredient transforms within hours to phosphonic acid, and it is not readily taken up by plants from soil. Therefore, although fosetyl-Al is described as systemic, the potential risk to bees based on this study is considered to be reflective of one application of 32 kg a.i./ha.
- Observation details were limited in the summary, and did not include length of study (exposure and observation period).

Most bee attractive crops on the Canadian labels can be sprayed between 4 and 4.48 kg a.i./ha (up to 4 applications per season). Therefore, the study represents a conservative exposure scenario since it was applied at 32 kg a.i./ha, with no observable effects.

Summary: Although the level of concern (RQ ≥ 0.4) was exceeded for acute oral toxicity for turf use (RQ ≤ 0.79) based on a single application of 9.6 kg a.i./ha, the lack of effects on bees based on the semi-field brood study indicate that risk is not expected at rates of up to 32 kg a.i./ha. Therefore, mitigation statements for pollinators are not required on the labels based on the current use pattern. Bees are not expected to be adversely affected from the use of fosetyl-Al on crops and turf at currently labelled rates in Canada.

Predators and parasites: Beneficial insects

Based on the data available for beneficial insects, the most sensitive species, a predatory arthropod, has an effect endpoint of $LR_{50} < 6$ kg a.i./ha, (69.3% mortality at 6 kg a.i./ha; 98.9% mortality at 15 kg a.i./ha). The maximum cumulative application rate for crop uses is 9 kg a.i./ha on leaf surfaces and will result in an RQ of > 1.5 (for use on spinach). The RQ is > 2.5 for use on turf, based on a use rate of 38.4 kg a.i./ha/yr and a 10-day foliar half-life, see Table 11. The LOC of 1 for tier II studies is exceeded.

Terrestrial Vertebrates

See Appendix IX, Tables 13-17 for details on the toxicity, exposure and risk to birds and mammals.

Birds

The nomogram results, indicating the concentration of pesticide (dry weight) on various food items, were used to determine the concentration of pesticide in the diet of birds and small wild mammals, and the estimated daily exposure (EDE). Exposure is dependent on the body weight of the organism and the amount and type of food consumed. In the screening level assessment, a set of generic body weights was used for birds (20, 100, 1000 g) and small wild mammals (15, 35, 1000 g) to represent a range of bird and small wild mammal species. For each body weight, the food ingestion rate (FIR; equivalent to food consumption) will be based on equations from Nagy (1987). It is noted that diets of animals can be highly variable from season to season as well as day to day. Furthermore, animals are often opportunists and if they encounter an abundant and/or desirable food source, they may consume large quantities of that food. For these reasons, the screening level assessment used relevant food categories for each size group consisting of 100% of a particular dietary item. These items included the most conservative residue values for plants, grains/seeds, insects, and fruits. A 100% diet of plants for the smallest sizes of birds and mammals was not included as this was considered unrealistic. No small birds or mammals in North America are known to eat a diet primarily of leafy plant material or grass; a small bird or mammal would need to consume unrealistically high amounts of leafy plant material or grass to meet its energy requirements.

The exposure in the diet of birds or mammals is calculated based on the following equation.

$$\text{EDE (mg a.i./kg bw/day)} = \frac{\text{FIR}}{\text{bw}} \times \text{EEC}$$

where:
FIR = food ingestion rate of indicator species in dry weight (kg dry weight per day)
bw = body weight (kg)
EEC = concentration of compound in dry diet (mg a.i./kg dry weight diet) [from Table 5-18].

When toxicity endpoints and EECs are compared in a RQ (where RQ = EEC/toxicity endpoint), both values must have the same units, either daily dose (mg a.i./kg body weight/day) or concentration (mg a.i./kg dry weight), and should match with regard to time scale if possible.

RQs are better based on daily dose in order to avoid bias due to different food intake rates between lab and field. Additionally, toxicity endpoints must be expressed as a daily dose in order to extrapolate toxicity information to species of different body weights, or from one species to another.

The acute oral LD_{50} for the Japanese quail of 4997 mg a.i./kg bw/day was divided by a factor of 10 to account for potential differences in species sensitivity. The adjusted acute oral LD_{50} of 499.7 mg a.i./kg bw/day was used to calculate the risk quotients to determine risk to wild birds. For use on spinach, the acute oral LOC is not exceeded. For use on turf, the acute LOC is exceeded for birds. The RQ is 1.53, 1.2 and 1.24 for small, medium and large size birds.

Chronic effects in birds were determined using the reproductive no observed effect level (NOEL) of 1500 mg a.i./kg diet (216 mg a.i./kg bw), the highest rate tested which resulted in no significant adverse effects in Japanese quail. However, a LOEL was not established in the above study, and the true NOEL is uncertain. The LOC was exceeded for bird reproduction for both spinach and turf application rates (RQs = 1.6-2.1 and 2.7-3.5, respectively). Given that no effects were observed at the maximum tested concentration and that a LOEL could not be determined, it is likely that the risk assessment is conservative. However, it should also be noted that only one bird species was tested instead of at least two, introducing some uncertainty to the risk assessment.

Chronic risk to birds is lower when considering off field EECs and/or mean EEC values. For example, for use on spinach, RQs are reduced by more than 10× off field (RQ $\leq$ 0.13) and by more than 50% based on mean EECs (RQ $\leq$ 1.18).

Mammals

The end-use product containing 80% fosetyl-Al has an LD_{50} of > 2000 mg/kg bw (>1600 mg a.i./kg bw) in, rats which is classified as slightly toxic. The acute oral LD_{50} in rats of > 1600 mg a.i./kg bw/day was divided by a factor of 10 to account for potential differences in species sensitivity. The adjusted acute oral LD_{50} of >160 mg a.i./kg bw/day was used to calculate the RQs to determine risk to small mammals. For use on spinach, the acute oral LOC is exceeded, with RQs of < 1.6-5.1 for small to medium sized mammals. For use on turf, the acute oral LOC is exceeded, with RQs of < 2.7-8.6 for small to medium sized mammals. For use on lettuce, the acute oral LOC is exceeded, with RQs of up to < 3 for medium sized mammals. If leafy foliage is considered as the sole food source, RQs range up to < 5.68 in this group. The smallest mammals, which are assumed to consume insects only, are not expected to be at risk.

Chronic effects in mammals were determined using the reproductive NOEL of 6000 ppm in diet (439 mg a.i./kg bw), which resulted in no significant effects. The LOEL was 12,000 ppm in diet, where effects on growth of offspring were noted. The LOC was exceeded for mammalian reproduction for both spinach and turf application rates (RQs up to 1.8 and 3.1, respectively). For use on lettuce, the chronic LOC is exceeded, with RQs of up to 2 for leafy foliage. Risk to mammals is significantly lower when considering off field EECs and mean EEC values. For example, for use on spinach, RQs are reduced by more than 10× off field (RQ $\leq$ 0.1) and by more than 50% based on mean EECs (RQ $\leq$ 0.7).

Terrestrial plants

See Appendix IX, Table 11 for details on the toxicity, exposure and risk to terrestrial plants. Fosetyl-Al in a formulated form product is not toxic to terrestrial plants at rates up to 80 kg a.i./ha (EC50 > 80 kg a.i./ha). The maximum seasonal rate is based on turf use (4 × 9600 = 38.4 kg a.i./ha) and does not exceed the LOC.

Summary: Fosetyl-Al may pose a risk to beneficial arthropods. A risk was also determined for acute and chronic effects on birds and chronic effects on small mammals. The proposed mitigation measures to reduce risk to beneficial arthropods and birds and mammals are label statements warning of toxicity to these organisms.

4.2.2 Risks to Aquatic Organisms

See Appendix IX, Tables 18-23 for details on the toxicity, exposure and risk to aquatic organisms.

Aquatic organisms could be exposed to the active from drift or runoff. At the screening level, EECs are calculated based on a direct application to water at the maximum cumulative rate, thus taking into account the maximum labelled application rate, the application interval and the dissipation of the compound in aquatic systems. Bodies of water of two depths are considered for the risk assessment. A depth of 15 cm is representative of a seasonal water body used by amphibians during the reproduction period. A depth of 80 cm is representative of a permanent water body for all other aquatic organisms.

The screening level EECs are based on the maximum seasonal application rate of 7 × 3.6 kg a.i./ha (spinach) and 4 × 9.6 kg a.i./ha (turf).From application on spinach, freshwater fish, amphibians and marine algae may be at risk based on a screening level scenario of overspray. For use on turf, freshwater fish, amphibians, marine algae and marine mollusks may be at risk using a screening level assessment.

Refined aquatic risk assessments were conducted for two spray drift scenarios. A runoff scenario based on water modelling was also used, see below.

For the aquatic eco-scenario assessment, EECs of fosetyl-Al from runoff into a receiving water body were simulated using the PRZM/EXAMS models. The PRZM/EXAMS models simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. The water body consists of a 1 ha wetland with an average depth of 80 cm and a drainage area of 10 ha. This water body is essentially a scaled down version of the permanent water body noted above, but having a water depth of 15 cm. However, in this case, only a seasonal water body was used as a refinement to assess the risk to amphibians, as the RQs were negligible at the screening level, and no risk was expected from concentrations in runoff. The peak concentrations in runoff based on application to spinach and turf were used to determine risk to aquatic organisms. Due to the very low concentrations of fosetyl-Al in runoff water, a risk to aquatic organisms was not identified for either of the high rate uses.

The risk to aquatic organisms from spray drift off the treated site was also assessed taking into consideration the drift deposition of spray of ASAE medium for ground boom (6%) and for airblast application (74%) at 1 m downwind from the site of application. The representative uses for these two spray drift scenarios were application on spinach (3600 g a.i./ha × 7) and apples (4000 g a.i./ha × 3).

For drift exposure from use on spinach, the LOC for amphibians is reached (RQ = 1.0) based on effects on early life-stage of fish. For drift exposure from use on apples, the LOC for fish is exceeded (RQ = 2.34). The LOC is also exceeded for amphibians based on early life-stage of fish (RQ = 12.5). Similarly, the LOC is exceeded for marine algae (RQ = 1.28). Based on the risks identified for fish spray buffer zones will be proposed to reduce exposure to acceptable levels.

Summary: For aquatic organisms, a risk was determined for freshwater fish and amphibians as well as marine mollusks and algae, based on screening level assessments. Runoff of this fungicide does not present a risk. However, spray drift from certain uses may result in the level of concern being exceeded for fish, amphibians, and marine algae.

The proposed mitigation measure to reduce risk to aquatic organisms such as fish, amphibians and invertebrates are spray buffer zones to prevent drift off field and generic label statements warning of toxicity to these organisms. In addition, label statements will be used to help reduce surface runoff.

4.3 Incident Reports - Environment

As of 10 July 2017, the PMRA received one major environmental incident report involving fosetyl-Al. In this incident, mortality was reported in a large number of non-schooling fish after water used to douse a pesticide warehouse fire overflowed into a creek. Several active ingredients reported in the incident, including fosetyl-Al, were not analyzed in the collected water samples. As such, there was insufficient information to further assess the role of fosetyl-Al in the reported fish mortality. A review of other chemicals that were detected in the water samples indicated that they are more toxic to fish (when compared to fosetyl-Al) and were possibly linked to the fish mortality. The USEPA Ecological Incident Information System (EIIS) was also queried for environment incidents. There were four incident reports available in the database. All four incidents involved plant damage to spinach and were considered either possibly or probably related to the applied pesticide. The incident data were considered into the re-evaluation of fosetyl-Al and no additional mitigation action is proposed.

5.0 Value

Fosetyl-Al is registered for use as a drench treatment and foliar spray to control fungal diseases on a number of food and feed crops, ornamentals and turf. Fosetyl-Al is particularly important for the management of root diseases caused by *Phytophthora* and *Pythium* species on apples, berries, ginseng, Belgian endives, brassica vegetable transplants and ornamentals, and downy mildew diseases caused by *Plasmopara*, *Peronospora* and *Hyaloperonospora* species on brassica vegetables, lettuce, onions, spinach and grapes. It is also important for the control of Pythium

diseases as well as foliar and basal rot anthracnose diseases on turf. Furthermore, fosetyl-Al is valuable for the management of a quarantine pest, sudden oak death caused by *Phytophthora ramorum*, in greenhouse and field grown ornamental plants and outdoor conifers. The other alternatives for the management of *Phytophthora ramorum* in susceptible ornamentals are metalaxyl-M and S-isomer and dimethomorph. Metalaxyl-M and S-isomer is at high risk for disease resistance development and resistance management is required.

For some other crops, fosetyl-Al has value where a limited number of alternatives are registered to manage the diseases. For example, metalaxyl-M and S-isomer is the only other fungicide registered for control of phytophthora crown and root rot on apples.

Resistance Management

Although there are a few resistance cases reported in certain pathogens, fosetyl-Al is still considered of low risk for resistance development. It is a completely systemic fungicide and is most effective when used as preventative treatments. It is effective as a rotational fungicide in an integrated pest management program with other fungicides belonging to different mode of action groups to delay the development of resistance in fungal pathogens.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, fosetyl-Al and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[1] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Fosetyl-Al does not meet Track 1 criteria, and is not considered a Track 1 substance. See Appendix IX, Table 24 for comparison with Track 1 criteria.
- Fosetyl-Al does not form any transformation products that meet all Track 1 criteria.

[1] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical grade active ingredient and formulants and contaminants in the end-use products are compared against the list maintained in the *Canada Gazette*.[2] The list is used as described in the PMRA Notice of Intent NOI2005-01[3] and is based on existing policies and regulations, including Regulatory Directives DIR99-03 and DIR2006-02,[4] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- The end-use products do not contain any formulants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through the PMRA formulant initiatives and DIR2006-02.

7.0 Conclusion

Fosetyl-Al provides control of various fungal diseases, mainly damping-off, root rot and downy mildew on a wide range of agricultural crops as well as on ornamentals and turf. Fosetyl-Al has a low risk for developing resistance in fungal diseases. It can be used in rotation with other mode of action fungicides, including fungicides that are at high risk for developing resistance, to help delay resistance development. In addition, fosetyl-Al is approved for use on ornamentals for the management of sudden oak death disease, a quarantine pest regulated in Canada.

With respect to human health, risks of concern were identified for certain occupational exposures to fosetyl-Al, resulting in the proposal to cancel uses on cut flowers and drench application to bedding plants is proposed. Additional mitigation measures are proposed for some of the remaining uses, including longer REIs. Exposure from these remaining uses is unlikely to affect human health when used according to the proposed label directions.

Fosetyl-Al enters the environment when used outdoors. It is unlikely to affect the environment when used according to the proposed label directions, which include advisory statements and spray buffer zones.

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2 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

3 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

4 DIR2006-02, *PMRA Formulants Policy, Formulants Policy and Implementation Guidance Document.*

List of Abbreviations

↑	increased
↓	decreased
♀	females
♂	males
°C	degree Celsius
µg	microgram(s)
µm	micrometer(s)
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handler Exposure Task Force
Al	aluminum
ARfd	acute reference dose
ARTF	Agricultural Re-Entry Task Force
ASAE	American Society of Agricultural Engineers
ATPD	area treated per day
BAF	bioaccumulation factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
bwg	body weight gain
Ca	calcium
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CG	crop group
Cl	chlorine
cm	centimetre(s)
cm^2	square centimeter(s)
CR	chemical resistant
d	day(s)
DACO	data code
DEEM	Dietary Exposure Evaluation Model
DER	Data Evaluation Record
DFR	dislodgeable foliar residue
DT_{50}	time required to observe a 50% decline in concentration
EC_{50}	median effective concentration
EDE	estimated daily exposure
EEC	estimated environmental concentration
EFED	Environmental Fate and Effects Division (USEPA)
EU	European Union
EUP	end-use product
F_0	parental animals
F_1	1st generation offspring
$F_{1a,b}$	1st generation offspring in two consecutive litters, a= first and b=second
F_2	2nd generation offspring

$F_{2a,b}$	2nd generation offspring in two consecutive litters, a= first and b=second
F_3	3rd generation offspring
$F_{3a,b}$	3rd generation offspring in two consecutive litters, a= first and b=second
FIR	food ingestion rate
FRAC	Fungicide Resistance Action Committee
g	gram(s)
ha	hectare(s)
hr	hour(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_d	soil-water partition coefficient
K_{oc}	organic carbon partition coefficient
K_{ow}	n-octanol/water partition coefficient at 25°C
L	litre(s)
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LR_{50}	median lethal rate
m	metre(s)
max	maximum
mg	milligram(s)
min	minute(s)
mL	millilitre(s)
MOA	mode of action
MOE	margin of exposure
mol	moles
mPa	millipascal(s)
MPHG	mechanically pressurized handgun
MPHW	manually pressurized handwand
MRID	Master Record Identifier Number (USEPA)
MRL	maximum residue limit
NIOSH	National Institute for Occupation Safety and Health
nm	nanometre(s)
N/A	not applicable
Na	sodium
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
P	phosphorus
PHED	Pesticide Handlers Exposure Database
PHI	pre-harvest interval
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	post-natal day
PPE	personal protective equipment

ppm	parts per million
REI	restricted-entry interval
RQ	risk quotient
S9	Mammalian metabolic activation system
SOP	standard operating procedures
$t_{1/2}$	half-life
TC	Transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WG	wettable granules
wk	week(s)
WP	wettable powder
wt	weight

Appendix I Registered Products Containing Fosetyl-Al[1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
24563	Technical	Bayer CropScience	Fosetyl-Al Technical	Dust or Powder	97%
24458	Commercial	Bayer CropScience	Aliette WDG Systemic Fungicide	Wettable Granules	80%
24564	Commercial	Bayer CropScience	Aliette Wettable Powder Systemic Fungicide	Wettable Powder	80%
27557	Commercial	Bayer CropScience	Chipco Aliette Ornamental Fungicide	Wettable Granules	80%
27688	Commercial	Bayer CropScience	Aliette Systemic Fungicide Water Dispersible Granule	Wettable Granules	80%
28299	Commercial	Bayer CropScience	Chipco Aliette Signature Fungicide	Wettable Granules	80%
32800	Commercial	Bayer CropScience	Signature XTRA Stressgard	Wettable Granules	60%

[1] As of 12 September 2017, excluding discontinued products or products with a submission for discontinuation

Appendix II Registered Commercial Uses of Fosetyl-Al in Canada

All information below is derived from product labels registered as of 24 February 2017, except for information provided by registrants which is indicated by [], and data calculated by the PMRA which is indicated by ().

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (a.i./ha)		Max Number Applications per Year	Min Interval between Applications (days)	Notes
				Maximum Single	Maximum Cumulative			
Use-site Category 5: Greenhouse Food Crops								
Brassica head and stem vegetable transplants - CG5-13 and Brassica leafy green transplants - CG4-13B	Damping-off (*Pythium* spp.)	Wettable granules	Ground application - drench	(2.4 kg/ha)	(4.8 kg/ha)	2	Not stated	
Lettuce – British Columbia only	Downy mildew	Wettable granules, Wettable powder	Ground application – foliar spray	(2.4 kg/ha)	(4.8 kg/ha)	2	14	
Use-site Category 6: Greenhouse Non-Food Crops and Use-site Category 27: Ornamentals Outdoor								
Ornamentals (Chinese evergreen (*Aglaonema*), *pothos*, *shefflera*, *spathiphilium*, *azalea*)	*Phytophthora* *Pythium*	Wettable granules, Wettable powder	Ground application - foliar spray	(2.24 kg/ha)	(6.72 kg/ha)	3	14	
Bedding plants - begonia, geranium, vinca, celosia, petunia, slavia and impatiens	*Phytophthora* *Pythium*	Wettable granules, Wettable powder	Ground application -foliar spray	(2.24 kg/ha)	(6.72 kg/ha)	3	14	
			Ground application - drench	(80 kg/ha)	(240 kg/ha)	3	30	
Ornamental plants and conifers	Sudden oak death (*Phytophthora ramorum*) - suppression	Wettable granules	Ground application -foliar spray	(4 kg/ha)	(16 kg/ha)	4	14	

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (a.i./ha)		Max Number Applications per Year	Min Interval between Applications (days)	Notes
				Maximum Single	Maximum Cumulative			
Use-site Category 13 and 14: Terrestrial Feed Crops and Terrestrial Food Crops								
Apples, non-bearing only - young trees without adequate foliage	Phytophthora crown and root rot	Wettable granules, Wettable powder	Ground – drench	(4 kg/ha)	(8 kg/ha)	2	Not stated	High density orchard
Apples - bearing only			Ground - foliar	(4 kg/ ha)	(12 kg/ha)	3	2nd application, 42 days later. 3rd application, soon after harvest.	Density greater than 750 trees/ha
Apples - Mutsu, Jonagold, Golden delicious	Blister spot		Ground - foliar	[2.0 kg/ ha]	(6.0 kg/ha)	3	7	
Use-site Category 14: Terrestrial Food Crops								
Belgian endive	Phytophthora root rot	Wettable granules	Ground - direct spray on roots for chicon production only.	(120kg/ha)	(120 kg/ha)	1	Not applicable	
Red/black raspberries blackberries	Phytophthora root rot	Wettable granules, Wettable powder	Ground application - foliar spray	[4.8 kg/ha]	[19.2 kg/ha]	4 (2 in the spring and 2 in the fall).	21	
Brassica head and stem vegetable – CG 5-13 and Brassica leafy green - CG4-13B)	Downy mildew (*Peronospora parasitica, Hyaloperonospora parasitica*)	Wettable granules, Wettable powder	Ground application - foliar spray	(2.5 kg/ha)	(12.5 kg/ha)	5	7	
Ginseng	Phytophthora foliar and root rot	Wettable granules, Wettable powder	Ground application - foliar spray	[4.4 kg/ha]	(22 kg/ha)	5	Not stated	
Highbush blueberries	Phytophthora root rot , anthracnose fruit rot, phomosis canker - suppression	Wettable granules	Ground application - foliar spray	(4.48 kg/ha)	(17.92 kg/ha)	4	14	

Site(s)	Pest(s)	Formulation Type	Application Methods and Equipment	Application Rate (a.i./ha)		Max Number Applications per Year	Min Interval between Applications (days)	Notes
				Maximum Single	Maximum Cumulative			
Lettuce	Downy mildew	Wettable granules, Wettable powder	Ground application - foliar spray	(2.24 kg/ha)	(11.2 kg /ha)	5	Not stated	
Onions	Downy mildew, purple blotch	Wettable granules, Wettable powder	Ground application - foliar spray	(2.24 kg/ha)	(11.2 kg/ha)	5	Not stated	
Spinach	Downy mildew (*Peronospora farinose* f. sp. *Spinaciae*) - suppression, Wwhite rust (*Albugo occidentalis*) - suppression	Wettable granules	Ground application - foliar spray	(3.6 kg/ha)	(25.2 kg/ha)	7	7	
Cranberry	Phytophthora root rot (*Phytophthora* spp.)	Wettable granules	Ground application - foliar spray	(4.4 kg/ha)	(17.6 kg/ha)	4	30	
Rutabaga	Downy mildew (Hyalop*eronospora parasitica*)	Wettable granules	Ground application - foliar spray	(2.5 kg/ha)	(12.5 kg/ha)	5	7	
Grapes, except table grapes	Downy mildew (*Plasmopara viticola*)	Wettable granules	Ground application - foliar spray	(3.0 kg/ha)	(21 kg/ha)	7	7	
Table grapes							12	
Strawberry	Red stele	Wettable powder	Ground application - foliar spray	(4.4 kg/ha)	(17.6 kg/ha)	4	30	
		Wettable granules		(4.48 kg/ha)	(17.92 kg/ha)			
Tobacco - flue-cured, burley, black	Blue mould	Wettable granules, Wettable powder	Ground application - foliar spray	(2.6 kg/ha)	(8.0 kg/ha)	4	7	
Use-site Category 30: Turf								
Turf - golf courses, sod farms, turf areas	Foliar and basal rot anthracnose Bentgrass deadspot	Wettable granules	Ground application - foliar spray	(9.6 kg/ha)	(38.4 kg/ha)	4	14	
Turf - golf courses, sod farms, turf areas	Pythium diseases	Wettable granules, Wettable powder	Ground application - foliar spray	(16 kg/ha)	(16 kg/ha)	1	Not applicable	

CG: crop group

Appendix III Toxicological Information for Health Risk Assessment

Table 1 Toxicity Profile of Technical Fosetyl-aluminum (Fosetyl-Al)

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted.

Study Type/Animal/PMRA #	Study Results
Absorption, distribution, Metabolism and elimination (gavage) Sprague Dawley Rats Organic portion of fosetyl-Al, O-ethyl phosphonic acid, used as a parent compound PMRA#1208730 PMRA#1208731 PMRA#1208677 PMRA#1208678 PMRA#1208679	**Single High Dose** **Absorption:** Absorption of fosetyl-Al was rapid (complete in ~10 hours) in rats following administration of a dose of 3000 mg/kg bw. **Distribution:** Approximately 9.4% of the administered dose (AD) was recovered in the tissues at 24 hours after the dose and the total radioactivity recovered at that point was 98.8% in males (♂) and 96.2% of the AD in females (♀). The highest residual radioactivity (TRR) at 7 days (0.78-1.4%) was found in the adrenal glands, gonads, spleen, kidneys, liver and brain. Neither parent nor metabolites were detected in the lipid, protein or water soluble fractions of the tissues. **Metabolism:** Fosetyl-Al underwent extensive metabolic transformation, with the major metabolite being CO_2. Only 0.5-2.2% of the parent compound and radiolabelled ethanol were found in urine, demonstrating that that a major portion of the absorbed dose underwent metabolic transformation. The suggested metabolic pathway was hydrolysis of fosetyl-Al into phosphite and ethanol. The phosphite metabolite was excreted directly via the urine while the ethanol was oxidized via acetaldehyde and acetate to CO_2-^{14}C. The acetate enters the 2-carbon metabolic pool for incorporation into radiolabelled normal cellular components. **Elimination:** Elimination of the radiolabel was 77% and 93% complete in 24 and 48 hours, respectively after a high single dose. Radiolabelled fosetyl-Al (C^{14}) was rapidly excreted in expired CO_2 (59-60% of AD), urine (27-36% of AD) and, faeces (2-3% of AD). Females excreted 3.3% of AD in the faeces and males excreted 1.9% in feces (after administration of a single high dose). Minimal amounts of fosetyl-Al in tissues at 7 days post-dosing (0.78-1.4% of AD). The rate of elimination was 30% faster in females than in males with a half-life ($t_{1/2}$) of 184h in males and 129 h in females. **Repeated Dose (7 Days):** Fosetyl-Al was extensively metabolised and excreted as CO_2 (60% of AD) following 7 days of dosing at 250 mg/kg bw/d. Twenty seven % of AD recovered in the urine after 24 hours consisted of 73% phosphite and 27% unchanged fosetyl-Al. Three to 4% of AD was recovered in the faeces, mainly consisting of phosphite metabolite. There was no evidence of unchanged fosteyl-Al in the carcass and only insignificant amounts of the phosphite metabolite in the carcass and intestinal tract after 24hrs (03.78%-0.67% ♂/♀). Remaining tissue residues were below the limits of detection, with the exception of residues in the kidneys and fat in females. **Main Metabolite – phosphorous acid as phosphite** Phosphite was adminsitered as sodium salt at 11 mg/kg bw for 7 days. Maximum

	concentration of radioactivity (%AD) in blood was reached at 1 - 2.5 hours after main metabolite dosing (in the form of sodium phosphite-^{32}P). The clearance of radioactivity from the blood seemed to occur in two stages. The first stage was fairly rapid with a half-life of 1 - 3 hours, while the second stage was much slower and a meaningful half-life could not be calculated. Phosphorous-^{32}P acid was excreted after repeat dosing (111 mg/kg bw/d) unchanged in the urine (59-65%) and the faeces (30-32%) with only 1 – 2% of the administered dose remaining in the carcass (highest in the spleen) at the end of 7 days.
Acute Toxicity Studies	
Acute oral toxicity SPF mice (strain not stated) Dunkin Hartley guinea pigs Beagle dogs PMRA #1208610	Mice: LD_{50} ♂ = 3340 mg/kg bw LD_{50} ♀ = 3750 mg/kg bw LD_{50} ♂♀ = 3460 mg/kg bw Clinical signs of toxicity: sedation, dyspnoea, prostration and death occurred within the first 24 hours at the highest doses. Congestion of glandular region of stomach was noted. Guinea Pigs: LD_{50} ♂ = approx. 2600 mg/kg bw LD_{50} ♀ = approx. 2600 mg/kg bw LD_{50} ♂♀ = approx. 2600 mg/kg bw Clinical signs of toxicity: sedation, dyspnoea and prostration were observed in animals at 3000 and 4500 mg/kg bw. Congestion of digestive tract was also noted. Dogs: No deaths; however, all animals vomited subsequent to dosing. The study is supplemental because no quantitative dose response can be established due to the unknown retained dose. **Low Toxicity**
Acute oral toxicity CD (COBS) rats Fauve de Bourgogne rabbits PMRA #1208611	Rats: LD_{50} ♂ = approx. 6000 mg/kg bw LD_{50} ♀ = approx. 5000 mg/kg bw LD_{50} ♂♀ = 5400 mg/kg bw (4005-6300 mg/kg bw) Clinical signs of toxicity: dyspnoea and sedation were observed 30 minutes after dosing and rats died after a period of depression. Marked congestion of the glandular region of the stomach and renal congestion was noted. Rabbits: LD_{50} ♂ = approx. 2500 mg/kg bw LD_{50} ♀ = approx. 2500 mg/kg bw LD_{50} ♂♀ = approx. 2500 mg/kg bw Clinical signs of toxicity: at the highest dose level, sedation and dyspnoea and delayed death. Marked congestion of the gastric mucosa with numerous petechiae and ulcerations was noted. **Low Toxicity**
Acute dermal toxicity Hy/Cr (NZW) albino rabbits PMRA #1208613	LD_{50} > 2000 mg/kg bw **Low Toxicity**
Acute inhalation toxicity SD rats	LC_{50} > 1.73 mg/L Transient clinical signs of toxicity: licking mouth (dust) and blinking; after four hours: prone, difficulty breathing, red discharge from snout, cold to touch; transient

PMRA #1208616	body wt loss. **Slightly acutely toxic**
Eye irritation Hy/Cr (NZW) albino rabbits PMRA #1208617	**Mildly irritating to the eye**
Dermal irritation H/Cv (NZW) rabbits PMRA #1208595	No edema or erythema observed **Non-irritating**
Dermal sensitization Hartley/Dunkin guinea pigs PMRA #1208596	Reactions following challenge with 1 mL 2% w/v were similar to dermal reactions during the induction phase. Inductions (3×week for 10 injections): 1: 0.05 mL 0.2% w/v saline 2 – 10: 0.1mL 0.2% w/v saline Challenge (2 weeks following last injection): 0.1 mL 0.2% w/v saline **Negative for sensitization**
Short-Term Toxicity Studies	
90d oral toxicity Sprague-Dawley rats PMRA #1208599	NOAEL 366/481 mg/kg bw/d 1922/2500 mg/kg bw/d: ↑ extramedullary haematopoiesis in spleen
30d oral toxicity (mechanistic study) C.O.B.S. rats PMRA #1208600	Study was designed to measure to examine calcium and phosphorus in the serum, urine and feces in rats. NOAEL for urinary tract effects = 580 mg/kg bw/d ≥ 1244/1376 mg/kg bw/d: ↑ urinary Ca excretion (calciuria), ↑ urinary P excretion (1st two weeks) (♂), ↓ P at end of treatment period; ↑ renal tubular changes (♂) composed of vacuolar degeneration of the epithelial cells of the renal tubules (distal convoluted tubules and straight parts of loop of Henle) with dose-related severity (cell necrosis and desquamation inside lumen were rarely observed) 2488/2885 mg/kg bw/d: ↑ urinary P excretion, ↑ faecal excretion of P; ↓ P (♀)
90d oral toxicity with 21 week recovery Sprague-Dawley (Crl:CD [SD] BR) rats PMRA #1230481, 1132292, 1146052	NOAEL = 539/649 mg/kg bw/d ≥ 2126/2459 mg/kg bw/d: ↑ uremia (↑ BUN), ↓ serum total protein, ↑ serum P & Ca, ↑ urinary volume, ↓ pH and specific gravity, ↓ urinary electrolytes (with exception of ↑ Ca and Al), ↑ faecal Al, ↑ urinary calculi; ↑ mortality, ↑ clinical signs, ↓ bw, ↓ water consumption, ↑ kidney wts, ↑ interstitial nephritis, hydronephrosis, transitional cell hyperplasia of kidney, urolith (kidney, ureter and urinary bladder), ureteritis, dilatation of ureter, papillary and transitional cell hyperplasia of urinary bladder, ↑ kidney and urinary bladder hyperplasia associated with urolithiasis (♂) 3529/4250 mg/kg bw/d: ↑ heme concentration secondary to diuresis, ↓ faecal Ca; ↑ rel thyroid wts (♂); ↑ clinical signs, ↓ bw, ↑ kidney wts, ↑ interstitial nephritis, hydronephrosis, transitional cell hyperplasia of kidney, urolith (kidney, ureter and

	urinary bladder), ureteritis, dilatation of ureter, papillary and transitional cell hyperplasia of urinary bladder, ↑ kidney and urinary bladder hyperplasia associated with urolithiasis (♀) Recovery: all changes recovered other than bw, kidney wts at 3529/4250 mg/kg bw/d
90d dietary toxicity Beagle dogs PMRA #1208602	NOAEL = 1309/1446 mg/kg bw/d No adverse effects (some animals vomited, including controls)
2 year dietary toxicity Beagle dogs PMRA #1208671	NOAEL (♂) = 309 mg/kg bw/d NOAEL (♀) = 1190 mg/kg bw/d ≥ 609/632 mg/kg bw/d: ↑ seminiferous tubule degeneration (♂) (spermatocyte and/or spermatidic giant cells in the lumen of the seminiferous tubules)
21d dermal toxicity NZW rabbits PMRA #1208603	NOAEL (irritation) = 380 mg/kg bw/d NOAEL (systemic toxicity) = 1500 mg/kg bw/d ≥ 750 mg/kg bw/d: slight to well-defined or moderate dermal irritation; ↑ acanthosis and inflammatory changes, hyperkeratosis
28d dermal toxicity Sprague Dawley rats PMRA# 2337299	LOAEL (dermal irritation) = 1050 mg/kg bw/d NOAEL (systemic toxicity) ≥ 1050 mg/kg bw/d 1050 mg/kg bw/day: acute inflammation at the site of treatment, ↑neutrophil counts, ↓ eosinophil counts (♀), hyperkeratosis , crusted areas macroscopically and erosions
Chronic Toxicity/Oncogenicity Studies	
2 year dietary chronic/oncogenicity toxicity CD rats PMRA #1208608,12086231, 1208623, 1208624, 1208660, 1208626	NOAEL = 88 mg/kg bw/d (♂) NOAEL = 450 mg/kg bw/d (♀) ≥ 348/450 mg/kg bw/d: ↑ incidence of urinary bladder inflammation (♂) 1372/1786 mg/kg bw/d: ↑ urinary bladder calculi and kidney calculi, ↑ hydronephrosis in kidney, ↑ urinary bladder inflammation (♂/♀); ↑ inflammation and transitional cell hyperplasia: urinary bladder transitional cell papilloma and combined bladder papilloma and carcinoma (♂); ↑ hydroureter incidence, ↑ kidney-pelvis papillocarcinoma and slight ↑ in bladder papillocarcinoma (♀) **Evidence of carcinogenicity at doses exceeding limit dose**
24-month dietary oncogenicity toxicity CD-1 mice PMRA #1208606	NOAEL = 3956/4550 mg/kg bw/d No adverse findings **No evidence of carcinogenicity**
Developmental/Reproductive Toxicity Studies	
Mutigenerational reproductive toxicity (dietary)	Parental NOAEL = 1153 mg/kg bw/d ≥ 994/1153 mg/kg bw/d: ↓ bwg of F2b, urinary tract lesions: F1, F2 (♂), F0 (♀),

CFY SPF rats PMRA #1208674	F1 (♀), F2 (♀)with crystalline or calcareous deposits in lumen of the urinary bladder frequently associated with minimal hyperplasia /hypertrophy of transitional epithelium sometimes associated with small papillary projections and/or desquamation of epithelial cells 2438/2514 mg/kg bw/d: ↑ chronic interstitial nephritis of both kidneys, deposits of mineral in the lumina of medullary collecting ducts and beneath transitional epithelium of the renal pelvis of one or both kidneys F1 and F2 (♂, ♀)and F0 (♀); ↑ mortality F1 and F2 (♂); ↓ bwg during lactation period (Day LD21 F1a, LD14&21 F1b, F2a, F2b and throughout lactation for F3a and F3b)(♀) Reproductive NOAEL ≥ 2438/2514 mg/kg bw/d No adverse effects Offspring NOAEL = 591 mg/kg bw/d Offspring LOAEL = 1153 mg/kg bw/d ≥ 994/1153 mg/kg bw/d: ↓ bw PND 12 and 21 F3a and b, 1 ♂ minimal hypertrophy of vesicular transitional epithelium of the bladder 2438/2514 mg/kg bw/d: ↓ bw PND 21 F1a and and b, F2a&b ↓ bw PND 12 in F3a&b ↓ bw PND 8 in F3b ↑ urinary bladder epithelial hyperplasia (associated with crystalline or calcareous deposits in the lumen, or serosa, mucoid epithelium or tubules of the seminal vesicle) F3b; ↑ lymph node hyperplasia F3b (♂); renal pelvic dilatation in F3ab (PND 21) **No evidence of sensitivity of the young**
Developmental toxicity (gavage) CFY SPF rats PMRA #1208673	Maternal NOAEL = 1000 mg/kg bw/d 4000 mg/kg bw/d: ↑ maternal mortality and clinical signs (chromodacryonrhea), gastric dilation and fluid retention, ↓ bwg, ↑ total resorptions Developmental NOAEL = 1000 mg/kg bw/d 4000 mg/kg bw/d: ↓ fetal/litter bws, ↑ skeletal and visceral malformations and variations (thoracic asymmetry, kidney displacement, renal pelvic cavitation, vein/artery transposition, displaced testes, abdominal and subcutaneous cranial haemorrhage) and sternebra variants (delayed ossification), hydrocephaly (considered equivocal), ↑ total resorptions (↓ litter size) **Evidence of malformations in excess of limit dose** **No sensitivity of the young**
Developmental toxicity (gavage) NZW rabbit PMRA #1208675 (French version)	Supplemental Maternal: ≥ 250 mg/kg bw/d: ↓bwg Developmental: No adverse findings **No evidence of malformations** **No evidence of sensitivity of the young**
Developmental toxicity (gavage)	Maternal NOAEL = 300 mg/kg bw/d No adverse effects

NZW rabbit PMRA#2337300	Developmental NOAEL = 100 mg/kg bw/d 300 mg/kg bw/day: ↑ incidence of distended ureter **No evidence of malformation** **Evidence of sensitivity of the young**
Range finding developmental toxicity (gavage) NZW rabbit PMRA# 2527065	Supplementary: Range finding study Maternal: ≥125 mg/kg bw/day: ↓bw, ↓bwg ≥250 mg/kg bw/day: bw loss GD 4-6, and ↑ post implantation loss, ↓ net wt change ≥500 mg/kg bw/day: 1 death (cause unknown), 1 humane sacrifice on GD 27 (hemorrhagic uterus); ↓ mean number of live fetuses (2 dead fetuses at this dose only) 1000 mg/kg bw/day: 1 humane sacrifice on GD 10 (fluid in stomach, discolored liver and ulceration), others sacrificed on GD 13 due to severe ↓ bw and fc; ↓ apparent pregnancy rate Developmental: ≥250 mg/kg bw/day: ↑ late resorption ≥500 mg/kg bw/day: ↓ mean # of live fetuses (2 dead fetuses at this dose only)
Genotoxicity Studies	
Micronucleus test PMRA #NA	**Negative**
In vivo chromosomal aberration Hydrated monosodium phosphite PMRA #1208667	**Negative**
Microbial point mutation (various tests) PMRA #1208676	AMES TA 1535, TA 1537, TA 1538, TA 98 and TA 100 ± S9 **Negative** Induct-test in E. coli K12 (λ), strain GY 5057 ± S9 **Negative** Yeast test (Saccharomyces cerevisiae D 7) for reverse mutation **Negative** DNA repair in E.coli **Negative**
Microbial point mutation PMRA #1208687	**Negative**
Metabolite Studies	
Acute oral toxicity OF1 SPF mice	**Mice:** Phosphorous acid: LD_{50} ♂ = 1600 mg/kg bw

CD (COBS) rats PMRA #1208612	LD_{50} ♀ = 1700 mg/kg bw LD_{50} ♂♀ = 1650 mg/kg bw Disodium phosphite: LD_{50} ♂ = 2.4 mg/kg bw LD_{50} ♀ = 2.5 mg/kg bw LD_{50} ♂♀ = 2.45 mg/kg bw **Rats:** Phosphorous acid: LD_{50} ♂ = 3250 mg/kg bw LD_{50} ♀ = 2850 mg/kg bw LD_{50} ♂♀ = 2905 mg/kg bw Disodium phosphite: LD_{50} ♂ = 5500 mg/kg bw LD_{50} ♀ = 5300 mg/kg bw LD_{50} ♂♀ = 5300 mg/kg bw Aluminum salt (fosetyl-Al): LD_{50} ♂ = 9500 mg/kg bw LD_{50} ♀ = 8200 mg/kg bw LD_{50} ♂♀ = 8900 mg/kg bw
3 month oral toxicity CD rats PMRA #1208601	Phosphorous acid as monosodium phosphite NOAEL = 150/180 mg/kg bw/d ≥ 330/370 mg/kg bw/day: ↑ excretion of Na^+ and Cl^-
2 year dietary toxicity CD rats PMRA #1208661, 1208665, 1208663	Monosodium phosphite Systemic NOAEL = 348/434 mg/kg bw/day 1482/1820 mg/kg bw/d: ↓ bw; ↑ incidence of soft stool (♂) **No evidence of carcinogenicity**
Microbial point mutation PMRA #1208699	Phosphorous acid as monosodium phosphite **Negative**
Microbial point mutation PMRA #1208710	Phosphorous acid **Negative** (Phage X development inhibited with 50 µg/plate in absence of metabolic activation only.)

Table 2 Toxicology Endpoints for Use in Health Risk Assessment for Fosetyl-Aluminum

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary All populations	Not established		
Repeated dietary All population	Chronic/carcinogenicity study in rats	NOAEL = 88 mg/kg bw/day Increased bladder inflammation in male rats	100
	ADI = 0.9 mg/kg bw/day		

Short-term/intermediate dermal[2] and inhalation	Developmental toxicity study in rabbit	NOAEL = 100 mg/kg bw/day distended ureter	100
long term dermal[2] and inhalation	Chronic/carcinogenicity study in rats	NOAEL = 88 mg/kg bw/day Increased bladder inflammation in male rats	100
Aggregate	Developmental toxicity study in rabbit	NOAEL = 100 mg/kg bw/day distended ureter	100
Cancer	Not considered to be carcinogenic in humans (below limit dose); threshold approach was deemed appropriate		

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments

[2] Since an oral NOAEL was selected, a dermal absorption factor 50% was used in a route-to-route extrapolation.

[3] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Appendix IV Dietary Exposure and Risk Estimates for Fosetyl-Al

Table 1 Dietary Exposure and Risk Estimates for Fosetyl-Al

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]			
			Food only		Food and drinking water	
	Dietary Exposure (mg/kg bw)	%ARfD	Dietary Exposure (mg/kg bw/day)	%ADI	Dietary Exposure (mg/kg bw/day)	%ADI
General Population (total)	Not applicable		0.146473	16	0.174658	19
All Infants (< 1 year old)			0.164244	18	0.269527	30
Children 1-2 years old			**0.401949**	**45**	**0.440711**	**49**
Children 3-5 years old			0.298895	33	0.330436	37
Children 6-12 years old			0.171825	19	0.195277	22
Youth 13-19 years old			0.100040	11	0.119910	13
Adults 20-49 years old			0.130116	14	0.158119	18
Adults 50+ years old			0.131505	15	0.158738	18
Females 13-49 years old			0.124412	14	0.151940	17

[1] Acute Reference Dose (ARfD) not established.
[2] Acceptable Daily Intake (ADI) of 0.9 mg/kg bw/day applies to all population subgroups.

Appendix V Food Residue Chemistry Summary

Metabolism in Livestock and Plants

Plant metabolism studies in four dissimilar crops, i.e. citrus, tomatoes, grapes and apples, as well as an animal metabolism study in goat were previously reviewed by the PMRA. The ^{14}C-labelled fosetyl-Al was used in all these studies. The degradation pathways in plants and animals are similar. Fosetyl-Al is comprised of aluminum and an organic portion, *O*-ethyl phosphonic acid. *O*-ethyl phosphonic acid breaks down to form two major metabolites, phosphonic acid (also called phosphorous acid) and ethanol. Ethanol leads to the formation of glucose and other natural products. One molecule of fosetyl-Al produces three molecules of phosphonic acid and the concentration of this metabolite is generally higher than that of the parent chemical. Lack of data from metabolism studies using ^{32}P-labelled fosetyl-Al precluded the quantification of phosphonic acid.

Based on the results observed in the animal and plant metabolism studies available to the PMRA, as well as evaluations from foreign reviews (EFSA, 2005; USEPA, 1990), the nature of the residue of the carbon moiety of fosetyl-Al in animals and plants is considered to be adequately understood. However, sufficient information is not available to full characterize the nature of the residue of phosphorus moiety of fosetyl-Al in both animals and plants.

Residue Definition

The current residue definition for fosetyl-Al in Canada is aluminum tris[ethyl phosphonate] for both risk assessment and enforcement purposes. No change is proposed to this residue definition for MRL enforcement as a result of this re-evaluation (i.e. the parent, fosetyl-Al per se, is a suitable marker for enforcement purposes). However, based on the toxicity of the metabolite phosphonic acid (i.e. assumed to have the same toxic potential as fosetyl-Al), the residue levels (i.e. more than 10% of the total radioactive residues and generally much higher than that of the parent chemical) and the criteria of the OECD guidelines, the residue definition for risk assessment is proposed to be revised to "aluminium tris(ethyl phosphonate) and its metabolite phosphonic acid, expressed as aluminium tris(ethyl phosphonate)" for plants, animals and drinking water.

Analytical Methodology

For plant commodities, adequate analytical methods have been developed for purposes of data gathering for the determination of both fosetyl-Al and phosphonic acid, as well as for enforcement for the determination of fosetyl-Al, using gas chromatography with flame photometric or thermionic detection (GC-FPD or GC-TID) and liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). For animal commodities, data gathering methods to detect both fosetyl-Al and phosphonic acid are available; however, enforcement methods to detect fosetyl-Al will need to be developed. Currently there is no multiresidue method in the United States Food and Drug Administration (USFDA)'s pesticide analytical methods volume I (PAM Vol. I) that can measure fosetyl-Al or phosphonic acid.

Magnitude of the Residue

Fosetyl-Al maximum residue limits (MRLs) have been established on the basis of adequate field trial residue data of this chemical for a range of crops/commodities. Established MRLs are accessible through Health Canada's MRL Database.

Most of the field trial studies measured the parent chemical, fosetyl-Al only. There are only four Canadian/US field trial studies (i.e. endives, peppers (bell and non-bell), apples and pineapple) in which both the parent chemical and the metabolite phosphonic acid were measured. Sufficient Canadian crop residue studies, in which phosphonic acid is further characterized in plants, are not available. These studies along with the required metabolism studies would be required to confirm the proposed revision of the residue definition. European field trial data, in which both the parent and metabolite are characterized, are available for a number of crops. To refine the chronic dietary risk assessment for fosetyl-Al and phosphonic acid, data were used from the available Canadian field trials and several EU field trials on crops that were identified as risk drivers when EU MRLs were used for the assessment (i.e. citrus, tomato, cucurbits eatable peel, grape and strawberry). Field trial data were translated from representative commodities in the crop group to other commodities within the crop group, where applicable.

Therefore, although limited, residue data or foreign reviews were available to conduct a dietary risk assessment for fosetyl-Al and phosphonic acid. However, further data including metabolism studies may be required for use expansion.

Crop Rotation Studies

There are no confined or field crop rotation trial studies on file for fosetyl-Al or phosphonic acid. However, recently available published literature or reviews indicated that transformation of phosphonic acid in soil is a slow process; therefore, it is possible that this chemical may remain in soil and be taken up by plants. Confined and field crop rotation trial studies on phosphonic acid may be required for further characterization of the nature of this chemical in soil and the rotational crops.

Processing Studies

Processing studies on file measured fosetyl-Al only and were previously reviewed. The experimental processing factors (PFs) are used in the refinement of the food dietary risk assessment for fosetyl-Al, as well as translation to phosphonic acid and used to refine the dietary risk assessment for fosetyl-Al and phosphonic acid. For commodities where experimental PFs are not available, theoretical PFs were used. Using processing factors of fosetyl-Al for phosphonic acid introduces uncertainties in the dietary exposure and risk assessment. Food processing studies on phosphonic acid may be required for the determination of the degradation or concentration of this chemical during processing.

Livestock and Milk Residue Data

Canadian MRLs have been established for residues of fosetyl-Al in animal commodities (*i.e.* cattle, goats, hogs, horses, sheep, and milk; see MRL Database). There are no registered/proposed uses for poultry feed items. Poultry feeding studies are not required for the current use pattern. Apple is a registered food crop of fosetyl-Al and it may be fed to livestock but it is considered as a minor feed item. In addition, residues of fosetyl-Al and phosphonic acid in animal commodities were not identified as dietary risk drivers or major contribution to the dietary exposure. Therefore, calculation of the maximum theoretical dietary burden (MTDB) is not necessary at this time.

Adequacy of the Food Residue Chemistry Database for Fosetyl-Al

Adequate data or foreign reviews were available to conduct a dietary risk assessment for fosetyl-Al and phosphonic acid. However, as discussed above, the current database does not meet the requirements of Dir98–02 "Residue Chemistry Guidelines" and Dir2010-05 "Revisions to the Residue Chemistry Crop Field Trial Requirements." For future use expansions, the following studies may be required.

DACO #	Study titles
6.2	Metabolism/Toxicokinetics Studies - Livestock
6.3	Metabolism/Toxicokinetics Studies - Plants
6.4	Metabolism/Toxicokinetics Studies - Other Studies/Data/Reports, if available
Rationale	The available plant and animal metabolism studies were conducted using ^{14}C-labelled fosetyl-Al only. Concentrations of the metabolite phosphonic acid are generally higher than those of the parent chemical. Lack of data from metabolism studies using ^{32}P-labelled fosetyl-Al precluded the quantification of phosphonic acid. Therefore, metabolism studies measuring both fosetyl-Al and phosphonic acid would be needed for confirmation of the understanding of the nature of residues of both the carbon and phosphorus moieties of fosetyl-Al.
7.2.2	Enforcement Analytical Methodology (Animal Commodities): Enforcement analytical methods to be developed for determination of fosetyl-Al in animal commodities.
7.2.3	An Inter-laboratory Analytical Methodology Validation: Inter-laboratory validation is required to evaluate a proposed enforcement method.
Rationale	Enforcement methods for detection of fosetyl-Al in animal commodities are not available, although MRLs have been established.
7.3	Freezer Storage Stability Tests on Phosphonic acid
7.4.1	Food and/or Feed Crop Residue Trial: Crop residue trial data measuring both fosetyl-Al and phosphonic acid.
7.4.2	Residue Decline: Residue decline studies on phosphonic acid
7.4.3	Confined Crop Rotation Trial: Confined crop rotation trial studies (or rationales) on phosphonic acid
7.4.4	Field Crop Rotation Trial: Field crop rotation trial studies (or rationales) on phosphonic acid

7.4.5	Processed Food/Feed: Food/feed processing studies on phosphonic acid
Rationale	Crop residue and freezer storage stability data of phosphonic acid would be required for further characterization of the residues of this metabolite in plant and animal commodities. These residue data will be used along with the required metabolism studies to confirm the proposed revision of residue definitions.

Appendix VI Residential Postapplication and Aggregate Risk Assessment

Table 1 Adult, Youth and Children Short-term Postapplication Exposure and Risk Assessments on Golf Courses

Scenario	TC[a] (cm^2/hr)	Duration (hours)	Dermal Exposure[b] (mg/kg bw /day)	Dermal MOE[c]
Adult	5300	4	0.27	360
Youth	4400	4	0.32	310
Children (6 to <11)	2900	4	0.38	270

MOE = Margin of Exposure, TC = transfer co-efficient; BW = Body Weight
[a] Transfer coefficient are based on the USEPA Residential SOPs (USEPA, 2012)
[b] Dermal Exposure (mg/kg bw/day) = (TTR (µg/cm^2) × TC (cm^2/hr) × Duration × DA)/BW (kg)
[c] Adult, youth and children short-term MOEs are based on a NOAEL of 100 mg/kg bw/day with a target MOE of 100.

Table 2 Adult, Youth and Children Short-term Postapplication Exposure and Risk Assessments for Trees and Retail Plants

Scenario	TC[a] (cm^2/hr)	Duration (hours)	Dermal Exposure[b] (mg/kg bw /day)	Dermal MOE[c]
Trees and retail plants[d]				
Adult	1700	1	0.278	359
Youth	1400	0.5	0.161	622
Children (6 to <11)	930	0.5	0.190	525

MOE = Margin of Exposure, TC = transfer co-efficient; BW = Body Weight
[a] Transfer coefficient are based on the USEPA Residential SOPs (USEPA, 2012)
[b] Dermal Exposure (mg/kg bw/day) = (DFR (µg/cm^2) × TC (cm^2/hr) × Duration × DA)/BW (kg)
[c] Adult, youth and children short-term MOEs are based on a NOAEL of 100 mg/kg bw/day with a target MOE of 100.
[d] Scenario applicable to outdoor and greenhouse bedding plants (begonia, geranium, vinca, celosia, petunia, slavia, and impatiens), ornamental plants (greenhouse container and field grown in nurseries and landscape plantings) and conifers grown in nurseries and landscape plantation), and greenhouse ornamentals (Chinese evergreen, pothos, shefflera, spathiphilium, azalea)

Table 3 Aggregate Risk Assessment

Population	Postapplication Scenario[a]	Dermal Exposure (mg/kg bw/day)[b]	Chronic Dietary (food and drinking water) Exposure (mg/kg bw/day)[c]	Total Exposure (mg/kg bw/day)[d]	Aggregate MOE[e]
Adult	Golfing	0.27	0.17	0.44	227
Youth		0.32	0.12	0.44	227
Children (6 to <11)		0.38	0.20	0.58	172
Adult	Trees and retail plants	0.28	0.17	0.45	222
Youth		0.16	0.12	0.28	357
Children (6 to <11)		0.19	0.20	0.39	256

MOE = Margin of Exposure

[a] Based on 4 applications with 14 day minimum interval between applications of fosetyl-Al.
[b] Dermal exposure (mg/kg bw/day) = Dermal exposure from postapplication exposure scenario on golfing courses and trees and retail plants.
[c] Dietary exposure values obtained from Appendix IV.
[d] Total Exposure (mg/kg bw/day) = (Dermal Exposure) + Chronic Dietary Exposure.
[e] Based on an oral NOAEL of 100 mg/kg bw/day and a target MOE of 100.

Appendix VII Occupational Mixer/Loader/Applicator Risk Assessment

Table 1 Occupational Mixer/Loader/Applicator Exposure and Risk Assessment

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
Personal Protective Equipment (PPE) specified on the current product labels: Coveralls, Chemical-resistant gloves (Mixer/Loader/Applicator)									
Airblast	WG	Apple (bearing)	4 kg/ha	20 ha	1723	30.9	58	3240	57
		Apple (bearing, Mutsu, Jonagold, Golden Delicious)	2 kg/ha	20 ha	861	15.4	116	6480	114
		Blackberry, red/black raspberry	4.8 kg/ha	20 ha	2067	37.1	48	2700	48
		Grapes	3 kg/ha	20 ha	1292	23.2	77	4320	76
		Highbush blueberries	4.48 kg/ha	20 ha	1930	34.6	52	2890	51
		Ornamental plants (field)	4 kg/ha	20 ha	1723	30.9	58	3240	57
	WP	Apple (bearing)	4 kg/ha	20 ha	1885	65.3	53	1530	51
		Apple (bearing, Mutsu, Jonagold, Golden Delicious)	2 kg/ha	20 ha	943	32.6	106	3060	103
		Blackberry, red/black raspberry	4.8 kg/ha	20 ha	2262	78.3	44	1280	43
Backpack	WG	Apple (non bearing; drench)	1.6 g/L	150 L	3.97	0.25	25200	397000	23700
		Bedding plants (drench)	0.758 g/L	150 L	1.88	0.12	53200	839000	50100
		Bedding plants (foliar)	11.2 g/L	150 L	27.8	1.76	3600	56800	3390
		Belgian endive	3 g/L	300 L	14.9	0.94	6720	106000	6320
		Blackberry, red/black raspberry	24 g/L	150 L	59.5	3.78	1680	26500	1580
		Bok choy (Chinese cabbage), Broccoli	16.7 g/L	150 L	41.4	2.63	2420	38100	2270
		Brassica leafy vegetables	16.7 g/L	150 L	41.4	2.63	2420	38100	2270
		Cranberry	29.3 g/L	150 L	72.6	4.61	1380	21700	1300
		Greenhouse broccoli and cabbage transplants	1.2 g/L	150 L	2.97	0.19	33600	530000	31600
		Greenhouse lettuce	1.2 g/L	150 L	2.97	0.19	33600	530000	31600
		Greenhouse ornamentals	11.2 g/L	150 L	27.8	1.76	3600	56800	3390
		Highbush blueberries	14.9 g/L	150 L	36.9	2.34	2710	42700	2550
		Lettuce (Field)	14.9 g/L	150 L	36.9	2.34	2710	42700	2550
		Onion	14.9 g/L	150 L	36.9	2.34	2710	42700	2550
		Ornamental plants (field)	4 g/L	150 L	9.91	0.63	10100	159000	9480
		Spinach	24 g/L	150 L	59.5	3.78	1680	26500	1580

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
		Strawberries	22.4 g/L	150 L	55.5	3.52	1800	28400	1690
		Tobacco (flue-cured, burley, black)	5.78 g/L	150 L	14.3	0.91	6980	110000	6560
		Turf (gold courses, sod farms, turf areas)	16 g/L	150 L	39.7	2.52	2520	39700	2370
	WP	Apple (non bearing; drench)	1.6 g/L	150 L	4.45	0.35	22500	282000	20800
		Bedding plants (drench)	0.758 g/L	150 L	2.11	0.17	47400	595000	43900
		Bedding plants (foliar)	11.2 g/L	150 L	31.2	2.48	3210	40300	2970
		Blackberry, red/black raspberry	24 g/L	150 L	66.8	5.32	1500	18800	1390
		Bok choy (Chinese cabbage), Broccoli	16.7 g/L	150 L	46.5	3.70	2150	27000	1990
		Greenhouse lettuce	1.2 g/L	150 L	3.34	0.27	29900	376000	27700
		Greenhouse ornamentals	11.2 g/L	150 L	31.2	2.48	3210	40300	2970
		Lettuce (Field)	14.9 g/L	150 L	41.5	3.31	2410	30300	2230
		Onion	14.9 g/L	150 L	41.5	3.31	2410	30300	2230
		Strawberries	22.4 g/L	150 L	62.3	4.97	1600	20100	1490
		Tobacco (flue-cured, burley, black)	5.78 g/L	150 L	16.1	1.28	6220	78000	5760
		Turf (gold courses, sod farms, turf areas)	26.7 g/L	150 L	74.3	5.92	1350	16900	1250
Chemigation	WG	Cranberry	4.4 kg/ha	140 ha	179	168	558	596	288
Groundboom [Small Area]	WG	Bedding plants (drench)	80 kg/ha	2 ha	60.8	47.0	1650	2130	928
		Bedding plants (foliar)	2.24 kg/ha	26 ha	22.1	17.1	4520	5850	2550
		Blackberry, red/black raspberry	4.8 kg/ha	26 ha	47.4	36.6	2110	2730	1190
		Bok choy (Chinese cabbage), Broccoli	2.5 kg/ha	26 ha	24.7	19.1	4050	5240	2280
		Brassica leafy vegetables	2.5 kg/ha	26 ha	24.7	19.1	4050	5240	2280
		Cranberry	4.4 kg/ha	26 ha	43.5	33.6	2300	2980	1300
		Ginseng	4.4 kg/ha	26 ha	43.5	33.6	2300	2980	1300
		Lettuce (Field)	2.24 kg/ha	26 ha	22.1	17.1	4520	5850	2550
		Onion	2.24 kg/ha	26 ha	22.1	17.1	4520	5850	2550
		Rutabaga	2.5 kg/ha	26 ha	24.7	19.1	4050	5240	2280
		Spinach	3.6 kg/ha	26 ha	35.6	27.5	2810	3640	1590
		Strawberries	4.48 kg/ha	26 ha	44.2	34.2	2260	2930	1280
		Tobacco (flue-cured, burley, black)	2.6 kg/ha	26 ha	25.7	19.8	3890	5040	2200
		Turf (gold courses, sod farms, turf areas)	9.6 kg/ha	30 ha	109	84.5	914	1180	516
		Turf (gold	16 kg/ha	30 ha	182	141	548	710	309

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
		courses, sod farms, turf areas)							
	WP	Bedding plants (drench)	80 kg/ha	2 ha	385	116	260	864	200
		Bedding plants (foliar)	2.24 kg/ha	2 ha	10.8	3.24	9270	30900	7130
		Blackberry, red/black raspberry	4.8 kg/ha	26 ha	301	90.3	333	1110	256
		Bok choy (Chinese cabbage), Broccoli	2.5 kg/ha	26 ha	157	47.0	639	2130	491
		Ginseng	4.4 kg/ha	26 ha	276	82.8	363	1210	279
		Lettuce (Field)	2.24 kg/ha	26 ha	140	42.1	713	2370	548
		Onion	2.24 kg/ha	26 ha	140	42.1	713	2370	548
		Strawberries	4.48 kg/ha	26 ha	281	84.3	356	1190	274
		Tobacco (flue-cured, burley, black)	2.6 kg/ha	26 ha	163	48.9	614	2040	472
		Turf (gold courses, sod farms, turf areas)	16 kg/ha	30 ha	1156	347	87	288	67 (Target MOE of 100 is met if the amount handled per day is limited to 320 kg a.i./day)
MPHG	WG	Apple (non bearing; drench)	1.6 g/L	3800 L	95.0	13.1	1050	7610	924
		Bedding plants (drench)	0.758 g/L	3800 L	45.0	6.22	2220	16100	1950
		Bedding plants (foliar)	11.2 g/L	3800 L	665	91.9	150	1090	132
		Blackberry, red/black raspberry	24 g/L	3800 L	1426	197	70	508	62
		Greenhouse broccoli and cabbage transplants	1.2 g/L	3800 L	71.3	9.85	1400	10200	1230
		Greenhouse lettuce	1.2 g/L	3800 L	71.3	9.85	1400	10200	1230
		Greenhouse ornamentals	11.2 g/L	3800 L	665	91.9	150	1090	132
		Highbush blueberries	14.9 g/L	3800 L	885	122	113	818	99 (rounded up to 100)
		Ornamental plants (field)	4 g/L	3800 L	238	32.8	421	3050	370
		Strawberries	22.4 g/L	3800 L	1331	184	75	544	66
		Tobacco (flue-cured, burley, black)	5.78 g/L	3800 L	343	47.4	291	2110	256
	WP	Apple (non bearing; drench)	1.6 g/L	3800 L	107	15.7	931	6350	812
		Bedding plants (drench)	0.758 g/L	3800 L	50.9	7.46	1970	13400	1710
		Bedding plants (foliar)	11.2 g/L	3800 L	752	110	133	907	116

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
		Blackberry, red/black raspberry	24 g/L	3800 L	1611	236	62	423	54
		Greenhouse lettuce	1.2 g/L	3800 L	80.5	11.8	1240	8470	1080
		Greenhouse ornamentals	11.2 g/L	3800 L	752	110	133	907	116
		Strawberries	22.4 g/L	3800 L	1503	220	67	454	58
		Tobacco (flue-cured, burley, black)	5.78 g/L	3800 L	388	56.9	258	1760	225
MPHW	WG	Apple (non bearing; drench)	1.6 g/L	150 L	1.17	0.20	85300	498000	72800
		Bedding plants (drench)	0.758 g/L	150 L	0.56	0.10	180000	1050000	154000
		Bedding plants (foliar)	11.2 g/L	150 L	8.21	1.41	12200	71100	10400
		Belgian endive	3 g/L	300 L	4.40	0.75	22700	133000	19400
		Blackberry, red/black raspberry	24 g/L	150 L	17.6	3.02	5680	33200	4850
		Bok choy (Chinese cabbage), Broccoli	16.7 g/L	150 L	12.2	2.10	8170	47700	6970
		Brassica leafy vegetables	16.7 g/L	150 L	12.2	2.10	8170	47700	6970
		Cranberry	29.3 g/L	150 L	21.5	3.68	4660	27200	3980
		Ginseng	22 g/L	150 L	16.1	2.76	6200	36200	5290
		Greenhouse broccoli and cabbage transplants	1.2 g/L	150 L	0.88	0.15	114000	663000	97100
		Greenhouse lettuce	1.2 g/L	150 L	0.88	0.15	114000	663000	97100
		Greenhouse ornamentals	11.2 g/L	150 L	8.21	1.41	12200	71100	10400
		Highbush blueberries	14.9 g/L	150 L	10.9	1.87	9160	53400	7820
		Lettuce (Field)	14.9 g/L	150 L	10.9	1.87	9160	53400	7820
		Onion	14.9 g/L	150 L	10.9	1.87	9160	53400	7820
		Ornamental plants (field)	4 g/L	150 L	2.93	0.50	34100	199000	29100
		Spinach	24 g/L	150 L	17.6	3.02	5680	33200	4850
		Strawberries	22.4 g/L	150 L	16.4	2.81	6090	35500	5200
		Tobacco (flue-cured, burley, black)	5.78 g/L	150 L	4.24	0.73	23600	138000	20200
	WP	Apple (non bearing; drench)	1.6 g/L	150 L	17.4	4.27	5760	23400	4620
		Bedding plants (drench)	0.758 g/L	150 L	8.22	2.02	12200	49400	9760
		Bedding plants (foliar)	11.2 g/L	150 L	121	29.9	823	3350	661
		Blackberry, red/black raspberry	24 g/L	150 L	260	64.0	384	1560	308
		Bok choy (Chinese cabbage), Broccoli	16.7 g/L	150 L	181	44.6	552	2240	443
		Ginseng	22 g/L	150 L	239	58.7	419	1700	336
		Greenhouse lettuce	1.2 g/L	150 L	13.0	3.20	7680	31200	6170

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
		Greenhouse ornamentals	11.2 g/L	150 L	121	29.9	823	3350	661
		Lettuce (Field)	14.9 g/L	150 L	162	39.8	619	2520	497
		Onion	14.9 g/L	150 L	162	39.8	619	2520	497
		Strawberries	22.4 g/L	150 L	243	59.8	412	1670	330
		Tobacco (flue-cured, burley, black)	5.78 g/L	150 L	62.7	15.4	1600	6480	1280
Turf gun	WG	Turf (gold courses, sod farms, turf areas)	16 g/L	3800 L	164.5	36.3	608	2753	498
Turf gun	WP	Turf (gold courses, sod farms, turf areas)	26.7 g/L	3800 L	242.2	194.0	413	515	229
Mitigation for scenarios which did not pass with the mid-level PPE as specified above (MOEs < the target MOE of 100) – by adding chemical-resistant hats for airblast applications and increasing level of PPE to the max-level PPE for MPHG.									
Coveralls, Chemical-resistant gloves (Mixer/Loader/Applicator); and Chemical resistant hat (Applicator).									
Airblast	WG	Apple (bearing)	4 kg/ha	20 ha	102	30.9	978	3240	751
		Blackberry, red/black raspberry	4.8 kg/ha	20 ha	123	37.1	815	2700	626
		Grapes	3 kg/ha	20 ha	76.7	23.2	1300	4320	1000
		Highbush blueberries	4.48 kg/ha	20 ha	115	34.6	873	2890	670
		Ornamental plants (field)	4 kg/ha	20 ha	102	30.9	978	3240	751
	WP	Apple (bearing)	4 kg/ha	20 ha	265	65.3	378	1530	303
		Blackberry, red/black raspberry	4.8 kg/ha	20 ha	317	78.3	315	1280	253
Chemical-resistant coveralls, Chemical-resistant gloves (Mixer/Loader/Applicator).									
MPHG	WG	Blackberry, red/black raspberry	24 g/L	3800 L	1064	197	94	508	79
		Strawberries	22.4 g/L	3800 L	993	184	101	544	85
	WP	Blackberry, red/black raspberry	24 g/L	3800 L	1235	236	81	423	68
		Strawberries	22.4 g/L	3800 L	1152	220	87	454	73
Mitigation for scenarios which did not pass with the max-level PPE as specified above (MOEs < the target MOE of 100) – by increasing spray volume to reduce potential exposure resulting from the use of MPHG, in addition to the mac level PPE requirement, Chemical-resistant coveralls, Chemical-resistant gloves (Mixer/Loader/Applicator).									
MPHG	WG	Blackberry, red/black raspberry	19.2 g/L (increased the minimum spray volume from 200 to 250 L/ha) [f]	3800 L	851	158	118	635	99 (rounded up to 100)
		Strawberries	17.92 g/L (need specify the minimum spray volume of 250 L/ha) [f]	3800 L	794	147	126	680	106
	WP	Blackberry, red/black raspberry	16 g/L (increased the minimum spray	3800 L	823	157	121	635	102

Application Method	Formulation	Crop	Application Rate [a]	Area treated per day	Exposure (µg/kg bw/day)		MOE		
					Dermal[b]	Inhalation[c]	Dermal[d]	Inhalation[d]	Combine[e]
			volume from 200 to 300 L/ha) [f]						
		Strawberries	14.93 g/L (need specify the minimum spray volume of 300 L/ha) [f]	3800 L	768	147	130	681	109

MOE = Margin of Exposure, MPHG = Mechanically Pressurized Handgun, MPHW = Manually Pressurized Handwand, WG = Wettable Granule, WP = Wettable Powder (Excluding WSP).

[a] Maximum application rates based on the current product labels.

[b] Dermal exposure (µg/kg bw/day) = (dermal unit exposure × ATPD × application rate × 50% refined dermal absorption)/80 kg body weight.

[c] Inhalation exposure (µg/kg bw/day) = (inhalation unit exposure × ATPD × application rate × 100% default dermal absorption)/80 kg body weight.

[d] MOE = NOAEL (mg/kg bw/day) / Exposure (mg/kg bw/day), based on a short-term toxicological endpoint established for dermal and inhalation rout of exposure. NOAEL of 100 mg/kg bw/day, target MOE = 100.

[e] Combined MOE = NOAEL (mg/kg bw/day) / (dermal exposure + Inhalation Exposure) (mg/kg bw/day).

[f] Refers to the proposed adjusted spray volume to mitigate risks of concern. To mitigate this potential risk, for blackberry and red/black raspberry, it is proposed to change the spray volume from 200-1000 L water/ha to 250-1000 L water/ha for wettable granule products and to 300-1000 L water/ha for wettable powder products. For strawberry, spray volumes are not specified on the current labels and; therefore, it is proposed to specify the minimum spray volume of 250 L water/ha for wettable granule products and 300 L water/ha for wettable powder products.

Appendix VIII Occupational Postapplication Risk Assessment

Table 1 Short-Term Postapplication Occupational Exposure and Risk Assessment

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (days)	REI specified on current labels (days)
						Peak	Disp	DFR_0	(days)	MOE [a]		
Apple (non bearing; drench)	4	2	90 [c]	Pruning, Scouting, Training	580	25%	10%	10.0	290	345	0.5	Do not re-enter treated area until residues have dried.
				Transplanting	230	25%	10%	10.0	115	869	0.5	
				Maintenance, Propping, Weeding	100	25%	10%	10.0	50.0	2000	0.5	
Apple (bearing only)	4	3	42 [d]	Thinning	3000	25%	10%	10.1	1518	66	4	Do not re-enter treated area until residues have dried.
				Harvesting	1400	25%	10%	10.1	708	141	0.5	
				Pruning, Scouting, Training	580	25%	10%	10.1	294	341	0.5	
				Transplanting	230	25%	10%	10.1	116	859	0.5	
				Maintenance, Propping, Weeding	100	25%	10%	10.1	50.6	1980	0.5	
Mutsu, Jonagold, Golden Delicious	2	3	7	Thinning	3000	25%	10%	8.54	1280	78	3	Do not re-enter treated area until residues have dried.
				Harvesting	1400	25%	10%	8.54	597	167	0.5	
				Pruning, Scouting, Training	580	25%	10%	8.54	248	404	0.5	
				Transplanting	230	25%	10%	8.54	98.2	1020	0.5	
				Maintenance, Propping, Weeding	100	25%	10%	8.54	42.7	2340	0.5	
Blackberry, red black raspberry	4.8	4	21	Irrigation (hand set)	1750	25%	10%	13.5	1179	85	2	Do not re-enter treated area until residues have dried.
				Harvesting, Tying/Training (Full)	1400	25%	10%	13.5	943	106	0.5	
				Pruning, Scouting, Tying/Training (Min), Weeding	640	25%	10%	13.5	431	232	0.5	
				Transplanting	230	25%	10%	13.5	155	645	0.5	
Brassica leafy vegetables (Broccoli raab (rapini), Bok choy (Chinese cabbage), Chinese broccoli (gai lon), Chinese mustard	2.5	5	7	Irrigation (hand set)	1750	25%	10%	11.7	1022	98 (rounded up to 100)	0.5	0.5
				Harvesting	1100	25%	10%	11.7	642	156	0.5	
				Transplanting	230	25%	10%	11.7	134	744	0.5	
				Scouting	210	25%	10%	11.7	123	815	0.5	

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (days)	REI specified on current labels (days)
						Peak	Disp	DFR	(days)	MOE [c]		
cabbage (Gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, Rape greens)				Thinning, Weeding	70	25%	10%	11.7	40.9	2450	0.5	
Brassica leafy vegetables (Broccoli, Brussels sprouts, Cauliflower, Cavalo broccolo)	2.5	5	7	Harvesting	5150	25%	10%	11.7	3008	33	11	0.5
				Scouting (Full), Weeding	4400	25%	10%	11.7	2570	39	9	
				Irrigation (hand set)	1750	25%	10%	11.7	1022	98 (rounded up to 100)	0.5	
				Scouting (Min), Thinning	1300	25%	10%	11.7	759	132	0.5	
				Transplanting	230	25%	10%	11.7	134	744	0.5	
Brassica leafy vegetables (Cabbage, Chinese cabbage (napa))	2.5	5	7	Weeding	4400	25%	10%	11.7	2570	39	9	0.5
				Irrigation (hand set)	1750	25%	10%	11.7	1022	98 (rounded up to 100)	0.5	
				Harvesting, MA-Harvesting, Scouting, Thinning	1300	25%	10%	11.7	759	132	0.5	
Ginseng	4.4	5	37 [a]	deflowering and hand picking seeds (berries) in ginseng	1100	25%	10%	11.2	618	162	0.5	Do not re-enter treated area until residues have dried.
				Irrigation (hand set)	1750	25%	10%	11.2	982	102	0.5	
				Transplanting	230	25%	10%	11.2	129	774	0.5	
				Scouting	210	25%	10%	11.2	118	848	0.5	
				Canopy Management, Weeding	70	25%	10%	11.2	39.3	2540	0.5	
Highbush blueberries	4.48	4	14	Irrigation (hand set)	1750	25%	10%	14.5	1267	79	3	1
				Harvesting	1400	25%	10%	14.5	1014	99 (rounded up to 100)	0.5	
				Bird Control, Frost Control, Pruning, Scouting, Weeding	640	25%	10%	14.5	463	216	0.5	
				Transplanting	230	25%	10%	14.5	167	600	0.5	
Lettuce	2.24	5	7 [a]	Irrigation (hand set)	1750	25%	10%	10.5	916	109	0.5	0.5
				Harvesting	1100	25%	10%	10.5	576	174	0.5	
				Transplanting	230	25%	10%	10.5	120	831	0.5	
				Scouting	210	25%	10%	10.5	110	910	0.5	
				Thinning, Weeding	70	25%	10%	10.5	36.6	2730	0.5	
Onion	2.24	5	7 [a]	Weeding	4400	25%	10%	10.5	2302	43	8	0.5
				Irrigation (hand set)	1750	25%	10%	10.5	916	109	0.5	

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (days)	REI specified on current labels (days)
						Peak	Disp	DFR_0	(days)	MOE [a]		
				Scouting, Thinning	1300	25%	10%	10.5	680	147	0.5	
Spinach	3.6	7	7	Irrigation (hand set)	1750	25%	10%	17.2	1501	67	4	0.5
				Harvesting	1100	25%	10%	17.2	943	106	0.5	
				Transplanting	230	25%	10%	17.2	197	507	0.5	
				Scouting	210	25%	10%	17.2	180	555	0.5	
				Thinning, Weeding	70	25%	10%	17.2	60.0	1670	0.5	
Cranberry	4.4	4	30	Harvesting (raking), Scouting	1100	25%	10%	11.5	632	158	0.5	0.5
				Transplanting	230	25%	10%	11.5	132	757	0.5	
				Pruning, Weeding	70	25%	10%	11.5	40.2	2490	0.5	
Rutabaga	2.5	5	7	Irrigation (hand set)	1750	25%	10%	11.7	1022	98 (rounded up to 100)	0.5	0.5
				Harvesting	1100	25%	10%	11.7	642	156	0.5	
				Scouting	210	25%	10%	11.7	123	815	0.5	
				Weeding	70	25%	10%	11.7	40.9	2450	0.5	
Grapes, wine juice	3	7	7	Harvesting, Leaf Pulling, Tying/Training	8500	25%	10%	14.3	6075	16	18	6
				Irrigation (hand set)	1750	25%	10%	14.3	1251	80	3	
				Bird Control, Propagating, Pruning, Scouting, Trellis Repair, Weeding	640	25%	10%	14.3	457	219	0.5	
				Transplanting	230	25%	10%	14.3	164	608	0.5	
Grapes, table	3	7	12	Girdling, Turning	19300	25%	10%	10.5	10085	10	22	Girdling or cane turning - 11 days, all other activities - 6 days.
				Harvesting, Leaf Pulling, Tying/Training	8500	25%	10%	10.5	4441	23	15	
				Irrigation (hand set)	1750	25%	10%	10.5	914	109	0.5	
				Bird Control, Propagating, Pruning, Scouting, Trellis Repair, Weeding	640	25%	10%	10.5	334	299	0.5	
				Transplanting	230	25%	10%	10.5	120	832	0.5	
Strawberries	4.48	4	30	Harvesting	1100	25%	10%	11.7	643	155	0.5	Do not re-enter treated area until residues have dried.
				Transplanting	230	25%	10%	11.7	135	743	0.5	
				Scouting	210	25%	10%	11.7	123	814	0.5	
				Canopy Management, Weeding	70	25%	10%	11.7	40.9	2440	0.5	
Tobacco (flue-cured, burley, black)	2.6	4	7	Irrigation (hand set)	1750	25%	10%	11.8	1033	97 (rounded up to 100)	0.5	Do not re-enter treated area until
				Canopy Management,	800	25%	10%	11.8	472	212	0.5	

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (days)	REI specified on current labels (days)
						Peak	Disp	DFR_0	(days)	MOE [a]		
				Harvesting, MA-Harvesting								residues
				Transplanting	230	25%	10%	11.8	136	736	0.5	have
				Scouting, Weeding	90	25%	10%	11.8	53.1	1880	0.5	dried.
Bedding plants (begonia, geranium, vinca, celosia, petunia, slavia and impatiens), field	2.24	3	14	Irrigation (hand set)	1750	25%	10%	7.17	628	159	0.5	Do not re-enter treated area until residues have dried.
Bedding plants (begonia, geranium, vinca, celosia, petunia, slavia and impatiens), Drench, field	80	3	30	Irrigation (hand set)	1750	25%	10%	209	18273	5	28 [g]	Do not re-enter treated area until residues have dried.
Bedding plants (begonia, geranium, vinca, celosia, petunia, slavia and impatiens), greenhouse	2.24	3	14	All activities	230	25%	2.3%	12.6	144	692	0.5	Do not re-enter treated area until residues have dried.
Bedding plants (begonia, geranium, vinca, celosia, petunia, slavia and impatiens), Drench, greenhouse	80	3	30	All activities	230	25%	2.3%	349	4014	25	60 [g]	Do not re-enter treated area until residues have dried.
Greenhouse broccoli and cabbage transplants	2.4	2	7 [f]	All Activities	230	25%	0%	12.0	138	725	0.5	Do not re-enter treated area until residues have dried.
Turf (gold courses, sod farms, turf areas)	9.6	4	14	All Activities	6700	1.0%	10%	1.24	416	240	0.5	Do not re-enter

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (days)	REI specified on current labels (days)
						Peak	Disp	DFR_0	(days)	MOE [a]		
												treated area until residues have dried.
Turf (gold courses, sod farms, turf areas)	16	1	0	All Activities	6700	1.0%	10%	1.60	536	187	0.5	Do not re-enter treated area until residues have dried.

DFR = Dislogeable Foliar Residue, Peak = Peak DFR as Percent of Rate, Disp = Percent Dissipation per Day, DFR_0 = Day 0 DFR (µg/cm^2), Exp = Exposure (µg/kg bw/day), MOE = Margin of Exposure, REI = Restricted-Entry Interval.

a. Dermal exposure (µg/kg bw/day) = DFR (µg/cm^2) × TC (cm^2/hr) × work duration (8 hr) × DA (Refined default 50%) / BW (80kg). Based on a short-term dermal NOAEL of 100 mg/kg bw/day and target MOE of 100; shaded cells indicate estimates of concern or the proposed REIs are not considered agronomically feasible. If target MOE is met, REI is set at 12 hours, or a statement about "spray is dried" for turf in golf courses.

b. Prolonged REIs are proposed for scenarios, which target MOE is not met.

c. For use on apple (non-bearing), application interval is not specified on the current labels. The labels indicate that "Make the first application in spring anytime after silver tip and again in early fall." Therefore, it is assumed that the application interval is 90 days.

d. For use on apple (bearing), application interval is not specified on the current labels. The labels indicate that "Treat from tight cluster to pink when there is sufficient leaf area present to take up the spray. Treat again approximately 6 weeks later. Treat again in the fall soon after harvest." Therefore, it is assumed that the application interval is 42 days.

e. For use on ginseng, application interval is not specified on the current labels. The labels indicate that "Make first application at full emergence. Repeat once between full emergence and seed set if environmental conditions require it. Apply again at seed set, once between seed set and pre-senescence (if required), final application at pre-senescence." Therefore, it is assumed that the application interval is 37 days.

f. Application interval is not specified on the current labels. It is assumed to be 7 days based on the application intervals for majority of the crops.

g. The proposed REIs are not considered feasible for this activity. Cancelation of handheld soil drench application is proposed and labels will be amended to mitigate potential risk. For more information see section 3.4.2 and Appendix X.

Table 2 Intermediate-Term Postapplication Occupational Exposure and Risk Assessment

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (Days)	REI specified on current labels (days)
						Peak	Disp.	DFR_0	Exp	MOE[a]		
Ornamental plants	4	4	14	Irrigation (hand set)	1750	25%	10%	12.9	1131	88	2	Do not re-enter treated area until
Ornamental plants	4	4	14	All other activities	230	25%	10%	12.9	149	672	0.5	
Ornamental plants (greenhouse)	4	4	14	All other activities	230	25%	2.3%	26.2	301	332	0.5	
Ornamental plants	4	4	14	Cut flower	4000	25%	10%	12.9	2586	39	9 [c]	

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (Days)	REI specified on current labels (days)
						Peak	Disp.	DFR_0	Exp	MOE [a]		
Ornamental plants (greenhouse)	4	4	14	Cut flower	4000	25%	2.3%	26.2	5239	19	71 [c]	residues have dried.

DFR = Dislogeable Foliar Residue, Peak = Peak DFR as Percent of Rate, Disp = Percent Dissipation per Day, DFR_0 = Day 0 DFR (µg/cm^2), Exp = Exposure (µg/kg bw/day), MOE = Margin of Exposure, REI = Restricted-Entry Interval.

a. Dermal exposure (µg/kg bw/day) = DFR (µg/cm^2) × TC (cm^2/hr) × work duration (8 hr) × DA (Refined default 50%) / BW (80 kg). Based on an intermediate-term dermal NOAEL of 100 mg/kg bw/day and target MOE of 100; shaded cells indicate estimates of concern or the proposed REIs are not considered agronomically feasible. If target MOE is met, REI is set at 12 hours.

b. Prolonged REIs are proposed for scenarios, which target MOE is not met.

c. The proposed REIs are not considered feasible for this activity. Cancelation of use on cutflowers is proposed and labels will be amended to mitigate potential risk. For more information see section 3.4.2 and Appendix X.

Table 3 Long-Term Postapplication Occupational Exposure and Risk Assessment

Crop	Maximum Application Rate (kg/ha)	Number of Applications per Season	Application Interval (days)	Activity	Transfer Coefficient (cm^2/hr)	Dislogeable Foliar Residue Inputs			Day 0 Estimates		Proposed REI [b] (Days)	REI specified on current labels (days)
						Peak	Disp.	DFR_0	Exp	MOE [a]		
Greenhouse lettuce	2.4	2	14	All Activities	230	25%	10%	12.0	138	638	0.5	Do not re-enter treated area until residues have dried.
Greenhouse ornamentals	4	3	14	All activities	230	25%	2.3%	22.4	258	341	0.5	Do not re-enter treated area until residues have dried.

DFR = Dislogeable Foliar Residue, Peak = Peak DFR as Percent of Rate, Disp = Percent Dissipation per Day, DFR_0 = Day 0 DFR (µg/cm^2), Exp = Exposure (µg/kg bw/day), MOE = Margin of Exposure, REI = Restricted-Entry Interval.

a. Dermal exposure (µg/kg bw/day) = DFR (µg/cm^2) × TC (cm^2/hr) × work duration (8 hr) × DA (Refined default 50%) / BW (80 kg). Based on a long-term dermal NOAEL of 88 mg/kg bw/day and target MOE of 100; shaded cells indicate estimates of concern. If target MOE is met, REI is set at 12 hours.

b. Prolonged REIs are proposed for scenarios, which target MOE is not met.

Table 4 Postapplication Exposure and Risk Assessment for Soil-contact Dermal Exposure Resulting from Use of Fosetyl-Al on Greenhouse Transplants and Bedding Plants

Scenario	Rate (kg a.i./ha)	Fraction a.i. available in upper 1 cm soil	CF (volume to weight conversion- cm^3/g soil)	Concentration in soil (mg a.i./mg soil) [a]	Adherence Factor (mg soil/cm^2-event) [b]	Skin surface area (cm^2)[c]	Dermal exposure (µg/kg bw/day)[d]	Margins of Exposure (MOE) [e]	Proposed Restricted-Entry Intervals (REIs) (days)[f]
Greenhouse broccoli and cabbage transplants	2.4	1	0.67	0.01608	0.5	3300	0.3317	3.0E+05	0.5
Bedding plants	80	1	0.67	0.53600	0.5	3300	11.0550	9.0E+03	0.5

[a] Concentration of fosetyl-Al in/on soil on the day of application (mg a.i./g soil). Value was estimated using the maximum rate for soil application and the assumption that 100% of the applied fosetyl-Al was located within the uppermost 1 cm of soil. Calculated using the following formula: Application rate (kg a.i./ha) * fraction of active ingredient in uppermost cm of soil (fraction/cm) assumed to be 100% * volume to weight conversion factor (0.67 cm^3/g soil).

[b] From the RAGS document (USEPA, 2004). There is not an activity specific-surface area weighted adherence factor for scouting with potential soil contact. Considering that lambda-cyhalothrin is applied in the early growth season and the onion seedlings and crown areas of the berry plants are the areas for inspection, commercial/industrial gardeners (adults) was selected as a central tendency (i.e. typical) soil contact activity and the high-end weighted adherence factor (i.e. 95th percentile) for that activity (0.5 mg/cm^2) was used.

[c] Surface area of exposed skin (head, hands, forearms) of 3300 cm^2. Value from the RAGS document (USEPA, 2004).

[d] Dermal exposure (µg/kg bw/day) = concentration in soil (µg a.i./mg soil) × adherence factor (0.5 mg soil/cm^2-event) × conversion factor (1×10^{-3} g/mg) × surface area (cm^2) × number of events/day × dermal absorption factor /body weight (80 kg). Based on the USEPA RAGS guidance document recommendations, a single event will be assumed. A dermal absorption (DA) factor of 50% was applied for the risk assessment.

[e] Based on a NOAEL of 100 mg/kg bw/day and a target dermal MOE of 100.

[f] The proposed Restricted-Entry Interval (REI) is the point in time when the target MOE of 100 was achieved.

Appendix IX Environmental Exposure and Risk Assessment

Table 1 Fate and Behaviour of Fosetyl-Al in the Terrestrial Environment

Property	Value	Major Transformation products	Comments	Reference
Abiotic transformation				
Hydrolysis	-pH5, 7, 9 = stable	None	Does not hydrolyse	EFSA 2005, PMRA 1996
Phototransformation in soil	NA	-	Not expected.	
Biotransformation				
Biotransformation in aerobic soil	DT_{50} Active: <1d	H_3PO_3: 157d Ethanol: 12-15hr	Active: Non-persistent H_3PO_3: moderately persistant	EFSA 2005, PMRA 1996, (PMRA 1208686)
Biotransformation in anaerobic soil	DT_{50} Active: 12-50 hrs	Ethanol: 12-15hr	Active: Non-persistent	EFSA 2005, PMRA 1996, (PMRA 1208691)
Mobility				
Adsorption / desorption in soil	Active: does not adsorb to soil	H_3PO_3: Kd=44-48 mL/g	Active: Not expected to be mobile under field conditions H_3PO_3: slightly mobile	EFSA 2005, PMRA 1996, PMRA 1208684, PMRA 1208685
Soil leaching	**<3.4% in leachate**	Ethanol: <36% in leachate H_3PO_3: None in leachate, bound to top 5cm soil	The active and its major product H_3PO_3 are not expected to leach under field conditions. Ethanol may leach in soils, but will dissipate rapidly.	EFSA 2005, PMRA 1996, PMRA 1208685, PMRA 1231263
Volatilization	NA	-	Not volatile	-
Field studies				
Field dissipation/ Field leaching	NA	-	-	-
NA: Not available or appropriate				

Table 2 Fate and Behaviour of Fosetyl-Al in the Aquatic Environment

Study type	Value	Major Transformation products	Comments	Reference
Abiotic transformation				
Hydrolysis	pH5, 7, 9 = stable	None	Stable, does not hydrolyse	EFSA 2005, PMRA 1996
Phototransformation in water	N/A	-	Not expected; does not absorb UV.	
Biotransformation				
Biotransformation in aerobic water systems	Active: 3.9-4.5d	Ethanol	Non-persistent	EFSA 2005, PMRA 1996
Biotransformation in anaerobic water systems	DT_{50} Active: 12-50	Ethanol: 12-15hr	Active: Non-persistent	EFSA 2005, PMRA 1996, PMRA

Study type	Value	Major Transformation products	Comments	Reference
(flooded soil)	hrs			1208691
Partitioning				
Adsorption / desorption in sediment	N/A	-	-	-
Bioconcentration	N/A	-	Not expected due to high solubility and low Kow.	-
Field studies				
Field dissipation	N/A			

N/A: Not available or appropriate.

Table 3 Estimated Environmental Concentrations of Fosetyl-Al and Phosphonic Acid in Potential Drinking Water Sources

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
Fosetyl-Al	0	0	1.7	0.18
Phosphonic acid	988	988	278	60

1 90th percentile of daily average concentrations
2 90th percentile of 365-day moving average concentrations
3 90th percentile of the peak concentrations from each year
4 90th percentile of yearly average concentrations

Table 4 Estimated Environmental Concentrations in Soil and Water

EECs for Use on Spinach (7 × 3600 = 25200 g a.i./ha, 7-day interval)		
Terrestrial EEC		
Soil	1.61mg a.i./kg soil	
Aquatic EEC Direct Overspray (µg a.i./L)		
15 cm	3640	
80 cm	683	
Aquatic EEC Off-field (µg a.i./L)		
	Drift	Runoff
15 cm	218	0.49
80 cm	41	0.092
EECs are based on highest application rate on spinach: 7 × 3600 g a.i./ha with 7-day interval. Soil EEC DT_{50} = 1d; DT_{50} water: 4.5d. Drift = 6% for ground boom use.		
EECs for Use on Turf (4 × 9600 = 38400 g a.i./ha, 14-day interval)		
Terrestrial EEC		
Soil	4.27 mg a.i./kg soil	
Aquatic EEC Direct Overspray (µg a.i./L)		
15 cm	7240	
80 cm	1357	
Aquatic EEC Off-field (µg a.i./L)		
	Drift	Runoff (µg a.i./L)
15 cm	434	0.24
80 cm	81	0.046
EECs are based on highest application rate on turf: 4 × 9600 g a.i./ha with 14 day interval. Soil EEC DT_{50} = 1d; DT_{50} water: 4.5d. Drift = 6% for ground boom use.		

Table 5 Major Groundwater and Surface Water Model Inputs for the Assessment of Fosetyl-Al and Phosphonic Acid

Type of Input	Parameter	Value	Phosphonic Acid
Application Information	Maximum allowable application rate per year (kg a.i./ha)	240 (bedding plants); 38.4 (turf); 25.2 (spinach)	N/A
	Maximum rate each application (kg a.i./ha)	80 (bedding plants); 9.6 (turf); 3.6 (spinach)	N/A
	Maximum number of applications per year	3 (bedding plants); 4 (turf); 7 (spinach)	N/A
	Minimum interval between applications (days)	7 (bedding plants); 14 (turf); 7 (spinach)	N/A
	Method of application	Foliar spray	N/A
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	Stable	Stable
	Photolysis half-life in water (days)	Stable	Stable
	Adsorption K_{oc} (mL/g)	0.1 (only value available)	2.3
	Aerobic soil biotransformation half-life (days) at 20°C	0.062 (slowest of four values)	Stable
	Aerobic aquatic biotransformation half-life (days) at 25°C	4.5 (only value available)	Stable
	Anaerobic aquatic biotransformation half-life (days) at 20°C	3.1 (slowest of two values)	Stable

Table 6 Aquatic Ecoscenario Modelling Estimated Environmental Concentrations for Fosetyl-Al in a Water Body 0.8-m Deep, Excluding Spray Drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Turf use, 4 × 9.6 kg a.i./ha, at 14-day intervals						
BC	0.019	0.016	0.010	0.005	0.004	0.001
Prairies	0.039	0.032	0.017	0.008	0.005	0.001
ON	0.026	0.021	0.009	0.004	0.003	0.001
QC	0.020	0.016	0.008	0.003	0.002	0.001
Atlantics	0.046	0.038	0.020	0.008	0.006	0.001
Maximum	**0.046**	**0.038**	**0.020**	**0.008**	**0.006**	**0.001**
Spinach use 7 × 3.6 kg a.i./ha, at 14-day intervals						
BC	0.009	0.008	0.005	0.003	0.002	0.001
Prairies	0.017	0.015	0.010	0.005	0.004	0.001
ON	0.069	0.058	0.035	0.022	0.018	0.004
QC	0.087	0.074	0.045	0.026	0.020	0.005
Atlantics	0.092	0.076	0.043	0.026	0.025	0.005
Maximum	**0.092**	**0.076**	**0.045**	**0.026**	**0.025**	**0.005**

Table 7 Aquatic Ecoscenario Modelling Estimated Environmental Concentrations for Fosetyl-Al in a Water Body 0.15-m Deep, Excluding Spray Drift

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Turf use, 4 × 9.6 kg a.i./ha, at 14-day intervals						
BC	0.10	0.084	0.051	0.024	0.021	0.004

Region	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Prairies	0.21	0.17	0.086	0.042	0.028	0.007
ON	0.14	0.11	0.048	0.022	0.015	0.004
QC	0.11	0.085	0.040	0.016	0.011	0.003
Atlantics	0.23	0.20	0.10	0.043	0.029	0.007
Maximum	**0.24**	**0.20**	**0.10**	**0.043**	**0.029**	**0.007**
Spinach use, 7 × 3.6 kg a.i./ha, at 14-day intervals						
BC	0.050	0.043	0.027	0.015	0.011	0.003
Prairies	0.091	0.081	0.053	0.028	0.019	0.005
ON	0.37	0.31	0.18	0.11	0.095	0.021
QC	0.46	0.39	0.23	0.14	0.10	0.026
Atlantics	0.49	0.40	0.22	0.14	0.13	0.025
Maximum	**0.49**	**0.40**	**0.23**	**0.14**	**0.13**	**0.026**

Table 8 Toxicity of Fosetyl-Al and its End-use Product to Terrestrial Organisms

Organism	Exposure	Endpoint value	Degree of toxicity[a]
Invertebrates			
Earthworms	Acute	TGAI: LC_{50} > 746-1000 mg a.i./kg soil EUP: LC_{50} of > 4000 mg product/kg soil H_3PO_3: LC_{50} >1000 mg a.i./kg soil	-
	Reproduction	NOEC = 1667 mg product/kg soil (1333 mg a.i./kg soil, as H_3PO_3 due to the short half-life of the parent chemical.)	
Bees	Oral	TGAI: LD_{50} = 462 µg a.i./bee TGAI: LD_{50} >400 µg a.i./bee EUP: LD_{50} > 440 ug product/bee. (>352 µg a.i./bee). H_3PO_3: LD_{50} > 212 µg/bee.	relatively non-toxic
	Contact	TGAI: LD_{50} >1000 µg a.i./bee TGAI: LD_{50} >200 µg a.i./bee EUP: LD_{50} > 390 µg product/bee (>312 µg a.i./bee). H_3PO_3: LD_{50} > 29.7 µg/bee.	relatively non-toxic
	Semi-field study with phacelia. Applied twice at a cumulative rate of 80 kg EUP/ha (64 kg a.i./ha). Applied before bees were introduced.	NOEC >32 kg a.i./ha (40kg product/ha) No colony level effects were observed for mortality, bee brood development or behavour.	-
Beneficial arthropods (80% WG, EUP)	Contact, Tier I., Mite *T. pyri*.	LR_{50} > 10 kg a.i./ha	-
	Contact, Tier I., Mite *T. pyri*.	LR_{50} < 9.6 kg a.i./ha (77.1% mortality @ 9.6 kg a.i./ha; 86.7% mortality @ 15 kg a.i./ha)	
	Contact, Tier I., Mite *T. pyri*.	LR_{50} > 15 kg a.i./ha	
	Contact, Tier II., Mite *T. pyri*.	LR_{50} < 6 kg a.i./ha (69.3% mortality @ 6 kg a.i./ha; 98.9% mortality @ 15 kg a.i./ha)	

Organism	Exposure	Endpoint value	Degree of toxicity[a]
	Contact. Tier I. Parasitic wasp *A. matricariae*	LR_{50} > 9.7 kg a.i./ha	
	Contact. Tier I. Parasitic wasp *A rhopalosiphi*	LR_{50} > 64 kg a.i./ha	
	Contact. Tier I. *P cupreus*	LR_{50} > 15 kg a.i./ha	
	Contact. Tier I. *C 7-punctata*	LR_{50} <15 kg a.i./ha (78.6% mortality @ 15 kg a.i./ha)	
	Contact. Tier I. *A bilineata*	LR_{50}: >15 kg a.i./ha	
Birds			
Bobwhite quail	Acute	TGAI: LD_{50} of >8000 mg a.i./kg bw EUP: LD_{50} of> 6400 mg/kg bw (>5120 mg a.i./kg bw) H_3PO_3: LD_{50} > 675 mg/kg bw	Practically non-toxic Slightly toxic
	Dietary	TGAI: LC_{50} > 20,000 mg a.i./kg feed H_3PO_3: >1692 mg /kg feed (>508 mg /kg bw)	Practically non-toxic Slightly toxic
Japanese quail	Acute	LD_{50} = 4997 mg a.i./kg bw	Practically non-toxic
	Reproduction	NOEL: 1500 mg a.i./kg feed (216 mg a.i./kg bw)	-
Mallard duck	Acute	-	-
	Dietary	LC_{50} > 20,000 mg a.i./kg feed	Practically non-toxic
	Reproduction	-	-
Mammals			
Rat	Acute	TGAI: LD_{50} > 7080 mg a.i./kg bw H_3PO_3: LD_{50} = 3624 mg/kg bw EUP: LD_{50} > 2000 mg/kg bw (>1600 mg a.i./kg bw)	Practically non-toxic Slightly toxic
	Dietary	366-580 mg a.i./kg bw/day (rats) 288-1309 mg a.i./kg bw/day (dogs)	-
	Reproduction	TGAI: NOEL = 6000 mg a.i./kg feed (439 mg a.i./kg bw); 524 mg a.i./kg bw/day H_3PO_3: NOEL = 8000 mg/kg feed (390 mg/kg bw)	-
Vascular plants			
Vascular plants	Seedling emergence[b]	NA	-
	Vegetative vigour[c]	EC_{50} > 80 kg a.i./ha	-

[a] Atkins et al. (1981) for bees and USEPA classification for others, where applicable. [b] shoot length. [c] shoot weight [d] European Commission, (2005). [e] SSD HC5 is the 5th percentile concentration derived from the Model: ETX 2; based on EC_{50} data sets.

Table 9 Toxicity of Fosetyl-Al and its End-use Product to Aquatic Organisms

Organism	Exposure/Species	Test material	Endpoint value (mg a.i./L)	Reference	Degree of toxicity[a] /Comment
Freshwater species					
Invertebrates					
Daphnia magna	Acute	TGAI EUP H_3PO_3	LC_{50}: >100; LC_{50}: 256; LC_{50}: 37 (29.6 a.i.) LC_{50}: >29.7	(EFSA, 2005) (PMRA 1231268) (EFSA, 2005) (EFSA, 2005)	Practically non-toxic Slightly toxic Slightly toxic
	Chronic	TGAI	NOEC: 17 (21d)	(EFSA, 2005) (PMRA 2337305)	-
chyronomid	*C. riparius*	H_3PO_3	NOEC: 100.2 (21d)	(EFSA, 2005)	-
Fiddler crab	Acute	TGAI	LC_{50}:145 LC_{50}:114	(PMRA 1208692); (US. EPA, 2014)	Practically non-toxic
Grass shrimp	Acute	TGAI	LC_{50}: 3.6	(PMRA 1208692)	Moderately toxic
Fish					
Rainbow trout	Acute	TGAI: EUP H_3PO_3	LC_{50}: > 122; LC_{50}: 92.2: 83.4 LC_{50}: > 120 (> 96 a.i.) LC_{50}: > 28.6	(EFSA, 2005); (PMRA 1208692); (US. EPA, 2014) (EFSA, 2005)	Practically non-toxic Slightly toxic Slightly toxic Slightly toxic
	Chronic	TGAI	NOEC: 100 (28d)	(EFSA, 2005)	-
Bluegill sunfish	Acute	TGAI H_3PO_3	LC_{50}: >60 LC_{50}: >150 LC_{50}: 141 LC_{50}: >35.7	(EFSA, 2005); (PMRA 1208692); (US. EPA, 2014) (EFSA, 2005);	Slightly toxic Practically non-toxic Slightly toxic
	Chronic	NA	-	-	-
Harlequin fish	Acute	TGAI	LC_{50}: 161.3	(PMRA 1208692)	Practically non-toxic
Fathed minnow	Sub-chronic (ELS)	TGAI	NOEC: 0.213	PMRA 2605095	-
Plants					
Freshwater alga	*Sc. subspicatus*	TGAI EUP	EbC50: 5.9 EbC50: 8.0 (6.4 a.i.)	(EFSA, 2005)	-
	S. capricornutum	TGAI H3PO3	EbC50: 4.99 EbC50: 8.6	(USEPA, 1990) (EFSA, 2005)	-
	Navicula pelliculosa	TGAI	EC_{50}: 8.93 EC_{50}: 4.2	(USEPA, 1990) (USEPA, 2014)	-
	Anabaena flos aquae	TGAI	EC_{50}: 7.24	(USEPA, 1990)	-
	Sc. pannonicus	TGAI	EC_{50}: 21.9	(PMRA 1208692)	-
	HC_5[b]	TGAI	2.75	PMRA	-
Vascular plant	Duck weed *Lemna gibba*	TGAI	EC_{50}: 79.7	(EFSA, 2005; USEPA, 2014)	-
Marine species					
Invertebrates					
Crustacean	Acute	-	-	–	-
	Chronic	-	-	-	-
Mollusk	Eastern oyster Acute	TGAI	EC50: 1.85	(USEPA, 2014)	Moderately toxic
	Chronic	-	-	-	-
Fish					
Sheepshead minnow	Acute	TGAI	LC_{50}: 122	(USEPA, 2014)	Practically non-toxic
Plants					
Marine alga	*Skeletonema costatum*	TGAI	EC50: 0.84 mg/L EC50: 0.78 mg/L	(USEPA, 1990); (USEPA, 2014)	-

a USEPA classification, where applicable; [b]SSD HC_5 is the 5[th] percentile effect concentration derived from the Model: ETX 2; based on EC_{50} data sets.

Table 10 Toxicity Endpoints Used in the Risk Assessment of Fosetyl-Al

Organism	Exposure	Endpoint	UF [1]	Adjusted Endpoint
Terrestrial Organisms				
Earthworm	acute	14-day LC_{50}. TGAI: LC_{50} > 746-1000 mg a.i./kg soil	2	14 day-LC_{50} >373 mg a.i./kg soil
Bee	oral	TGAI: LD_{50}= 462 µg a.i./bee EUP: LD_{50}> 440 ug product/bee. (>352 µg a.i./bee). H_3PO_3: LD_{50}> 212 µg/bee.	1	TGAI: LD_{50} = 462 µg a.i./bee EUP: LD_{50}> 440 µg product/bee. (>352 µg a.i./bee). H_3PO_3: LD_{50}> 212 µg/bee
	contact	48h-LD_{50} : TGAI: LD50 >1000 µg a.i./bee EUP: LD_{50}> 390 product/bee (>312 µg a.i./bee). H_3PO_3: LD_{50}> 29.7 µg/bee.	1	TGAI: LD_{50}>1000 µg a.i./bee EUP: LD_{50}> 390 µg product/bee (>312 µg a.i./bee). H_3PO_3: LD_{50}> 29.7 µg/bee.
	Semi-field study with *phacelia*. Applied twice at a cumulative rate of 80 kg EUP/ha (64 kg a.i./ha). Applied before bees were introduced.	NOEC >32 kg a.i./ha (40kg product/ha) No colony level effects were observed for mortality, bee brood development or behavour.	-	-
Beneficial Insects	Contact, Tier II., Mite T. pyri.	EUP (80WP) : LR_{50} < 6 kg a.i./ha (69.3% mortality @ 6 kg a.i./ha; 98.9% mortality @ 15 kg a.i./ha)	1	LR_{50} < 6 kg a.i./ha
Birds	Acute	TGAI: LD_{50} of >8000 mg a.i./kg bw; LD_{50} = 4997 mg a.i./kg bw EUP: LD_{50} of> 6400 mg/kg bw (>5120 mg a.i./kg bw) H_3PO_3: LD_{50} > 675 mg/kg bw	10	TGAI: LD_{50} = 499.7 mg a.i./kg bw H_3PO_3: LD_{50} > 67.5 mg/kg bw
	Reproduction	NOEL: 1500 mg a.i./kg feed (216 mg a.i./kg bw)	-	NOEL: 216 mg a.i./kg bw
Mammals (Rat)	Acute	TGAI: LD_{50} > 7080 mg a.i./kg bw EUP: LD_{50} > 2000 mg/kg bw (>1600 mg a.i./kg bw) H_3PO_3: LD_{50} = 3624 mg/kg bw	10	EUP: LD_{50} >160 mg a.i./kg bw
	Reproduction	TGAI: NOEL = 6000 mg a.i./kg feed (439 mg a.i./kg bw); 524 mg a.i./kg bw/day H_3PO_3: NOEL = 8000 mg/kg feed (390 mg/kg bw)	1	TGAI: NOEL = 439 mg a.i./kg bw
Terrestrial vascular plants	Seedling emergence	7d-EC_{50}	1	NA
	Vegetative vigour	EC_{50} > 80 kg a.i./ha	1	EC50 > 80 kg a.i./ha
Freshwater Organisms				
Daphnia magna	Acute	EUP: LC_{50} = 29.6 mg a.i./L H_3PO_3: LC_{50} >29.7 mg/L	2	LC_{50} = 14.8 mg a.i./L H_3PO_3: LC_{50} >14.8mg/L
	Chronic	21d-NOEC: 17 mg a.i./L	1	NOEC = 17 mg a.i./L

Organism	Exposure	Endpoint	UF [1]	Adjusted Endpoint
Grass shrimp	Acute	TGAI: LC_{50}: 3.6 mg a.i./L	2	LC_{50} = 1.8 mg a.i./L
Rainbow trout	Acute: TGAI. H_3PO_3	LC_{50} = 83.4 mg a.i./L LC_{50}: > 28.6 mg a.i./L	10	LC_{50} = 8.3 mg a.i./L LC_{50} > 2.86 mg a.i./L
	Chronic	NOEC	1	NA
	ELS	28d-NOEC = 100 mg a.i./L	1	100 mg a.i./L
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	1	NOEC = 0.213mg a.i./L
Amphibians (based on fish)	Acute	LC_{50} = 83.4 mg a.i./L	10	LC_{50} = 8.3 mg a.i./L
	ELS	32d-NOEC = 0.213 mg a.i./L	1	NOEC = 0.213 mg a.i./L
Aquatic vascular plants (*Lemna sp*)	Acute	TGAI: EC50: 79.7 mg a.i./L	2	40 mg a.i./L
Algae	Acute	TGAI: HC_5 = 2.75 mg a.i./L (Based on SSD for 5 sp).	-	HC_5 = 2.75 mg a.i./L
Marine organisms				
Saltwater invertebrates Eastern Oyster	Acute	TGAI EC_{50}: 1.85	2	0.93 mg a.i./L
	Chronic	NOEC	1	NA
Saltwater fish Sheepshead minnow	Acute	TGAI LC_{50}: 122 mg a.i./L	10	LC_{50} = 12.2 mg a.i./L
	Chronic	NOEC	1	NA
Saltwater algae *Skeletonema sp.*	Acute	EC_{50}: 0.78 mg a.i./L	2	0.39 mg a.i./L

[1] as per EAD standard uncertainty factor (UF); [2] An UF of 2 was applied to this endpoint as greater than 50% adverse effect was observed at the lowest test rate of 6 kg a.i./ha.

Note, RQs are designated as (<) less than values due to LD_{50} value for H_3PO_3 being ">".

Application rates used in RA: Risk was determined for crop uses based on the highest application rate on spinach (3600 g a.i./ha x 7 applications by ground boom sprayer). Risks associated with turf use were also determined where appropriate and risk to small mammals was investigated for use on lettuce (9600 g a.i./ha × 4 or 2240 g a.i./ha × 5 applications, respectively, by ground boom sprayer).

Table 11 Risk to Terrestrial Invertebrates and Plants

EECs based on A: turf use (4 × 9600 = 38.4 kg a.i./ha) or B: spinach use (7 × 3600 = 25.2 kg a.i./ha).

Organism	Exposure	Endpoint	Adjusted Endpoint[3]	EEC	RQ[1]	LOC[2] Exceeded
Invertebrates						
Earthworm	Acute	14-day LC_{50} TGAI: LC50 > 746-1000 mg a.i./kg soil	LC_{50} > 373 mg a.i./kg soil	A: 4.27 mg a.i./kg soil	<0.1	NO
Predatory arthropod Parasitic arthropod	Contact	EUP (80WP) : LR50 < 6 kg a.i./ha (69.3% mortality @ 6 kg a.i./ha; 98.9% mortality @ 15 kg a.i./ha)	LR_{50} < 6 kg a.i./ha	A: EUP=38.4 kg a.i./ha B: EUP=25.2 kg a.i./ha	**>6.4** **>4.2**	**YES** **YES**
Vascular plants						
Vegetative vigour	Foliar	EC50 > 80 kg a.i./ha	EC50 > 80 kg a.i./ha	A: EUP = 38.4 kg a.i./ha	<0.48	NO

[1]Risk Quotient (RQ) = exposure/toxicity

[2]Level of Concern (LOC) Shaded cells indicate that the RQ exceeds the LOC.

[3]Adjusted endpoint has an uncertainty factor applied as per EAD protocol, see Table 3.4-1

Note, RQs are designated as (<) less than values due to LD50 being ">".

Table 12 Risk to Bees

Based on application to spinach, turf or berry crops.

Organism	Exposure	Toxicity Endpoint value	EEC [a, b, c] µg a.i./bee	RQ	LOC exceeded?
Screening level					
Bee	Contact	Active: 48-h LD_{50} > 1000 µg a.i./bee	8.6-23	<0.009-0.023	No
		EUP: 48-h LD_{50} >312 µg a.i./bee		<0.03-0.07	No
		H_3PO_3: 48-h LD_{50} >29.7 µg a.i./bee	1.99-5.3	<0.07-0.18	No
	Oral	Active: 48-h LD_{50} : 462 µg a.i./bee	104.4-278.4 (spinach and turf[f])	0.23-0.6	**YES**
		EUP: 48-h LD_{50} >352 µg a.i./bee		<0.3-0.79	**YES**[e]
		Active: 48-h LD_{50} : 462 µg a.i./bee	130 (berry crops)	0.28	No
		EUP: 48-h LD_{50} >352 µg a.i./bee		<0.37	No
		H_3PO_3: 48-h LD_{50} >212 µg a.i./bee	24.1-64.3 (spinach and turf[f])	<0.11-0.3	No
Higher tier summary					
Bee colony Semi-field study with flowering plant *Phacelia sp.* Applied twice at a cumulative rate of 80 kg EUP/ha (64 kg a.i./ha); applied before sowing and at 30% flowering, before bees were introduced.		Summary: NOEC >32 kg a.i./ha (1x)* No colony level effects were observed for mortality, bee brood development or behaviour. *See section 3.4.2.1 for uncertainties.	n/a	n/a	n/a

NOTE: The acute EEC for bees is based on a single application rate due to flowers likely exposed only once for acute exposure and effects.

[a] An EEC for bees is calculated by multiplying a single application rate of interest, in units of kg a.i./ha by a standard factor of 2.4 µg a.i./bee for contact toxicity, and by a factor of 29 µg a.i./bee for oral toxicity which gives an EEC in units that match the toxicity endpoint (µg a.i./bee).

[b] The EEC for the transformation product H_3PO_3 is based on the assumption of 100% conversion from the active with a 23.1% residual rate (based on molar mass vs. parent).

[c] Application rates used to determine risk: spinach (3.6kg a.i./ha), turf (9.6 kg a.i./ha) and berry crops (4.48 kg a.i./ha).

[e] Risk is assumed to be up to indicated value as toxicity results were "<".

[f] Spinach and turf (i.e. sod) do not represent bee attractive crops, as such, limited exposure is expected. Note that other turf areas which may be treated by fosetyl-Al may contain clover or flowering plants which are bee attractive, however, based on a semi-field study, a risk to bees is not expected (see section 4.2.1).

Table 13 Risk to Birds - Spinach

Risk to birds was determined based on the acute EUP LD50 > 512 mg a.i./kg bw and reproductive NOEL = 216 mg a.i./kg bw, use rate of 3600 g a.i./ha × 7, foliar DT_{50} = 10d^.

Toxicity (mg a.i./kg bw/d)		Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	<512.0	Insectivore (small insects)	456.11	<0.89
Reproduction	216.0	Insectivore (small insects)	456.11	**2.11**
Medium Sized Bird (0.1 kg)				
Acute	<512.0	Insectivore (small insects)	355.95	<0.70
Reproduction	216.0	Insectivore (small insects)	355.95	**1.65**
Large Sized Bird (1 kg)				

Toxicity (mg a.i./kg bw/d)		**Feeding Guild (food item)**	**EDE** (mg a.i./kg bw)	**RQ**
Acute	<512.0	Herbivore (short grass)	371.41	<0.73
Reproduction	216.0	Herbivore (short grass)	371.41	**1.72**

^Foliar DT_{50} assumed to be 10d.

Table 14 Risk to Birds - Turf

Risk to birds was determined based on the acute EUP LD50 > 512 mg a.i./kg bw and reproductive NOEL = 216 mg a.i./kg bw, use rate of 9600 g a.i./ha × 4, foliar DT_{50} = 10d^.

Toxicity (mg a.i./kg bw/d)		**Feeding Guild** (food item)	**EDE** (mg a.i./kg bw)	**RQ**
Small Bird (0.02 kg)				
Acute	499.7	Insectivore (small insects)	762.87	**1.53**
Reproduction	216.0	Insectivore (small insects)	762.87	**3.53**
Medium Sized Bird (0.1 g)				
Acute	499.7	Insectivore (small insects)	595.34	**1.19**
Reproduction	216.0	Insectivore (small insects)	595.34	**2.76**
Large Sized Bird (1 kg)				
Acute	499.7	Herbivore (short grass)	621.21	**1.24**
Reproduction	216.0	Herbivore (short grass)	621.21	**2.88**

Table 15 Risk to Small Mammals - Spinach

Risk to mammals was determined based on the acute EUP LD_{50} > 160 mg a.i./kg bw and reproductive NOEL = 439 mg a.i./kg bw, use rate of 3600 g a.i./ha × 7, foliar DT_{50} = 10d^.

Toxicity (mg a.i./kg bw/d)		**Feeding Guild** (food item)	**EDE** (mg a.i./kg bw)	**RQ**
Small mammal (0.015 kg)				
Acute	<160.0	Insectivore (small insects)	262.34	**<1.64**
Reproduction	439.0	Insectivore (small insects)	262.34	0.60
Medium Sized Mammal (0.035 kg)				
Acute	<160.0	Herbivore (short grass)	821.91	**<5.14**
Reproduction	439	Herbivore (short grass)	821.91	**1.87**
Large Sized Mammal (1kg)				
Acute	<160.0	Herbivore (short grass)	439.18	**<2.74**
Reproduction	439.0	Herbivore (short grass)	439.18	**1.00**

^Foliar DT_{50} assumed to be 10d.

Table 16 Risk to Small Mammals - Turf

Risk to mammals was determined based on the acute EUP LD_{50} > 160 mg a.i./kg bw and reproductive NOEL = 439 mg a.i./kg bw, the use rate of 9600 g a.i./ha × 4, foliar DT_{50} = 10d^ .

Toxicity (mg a.i./kg bw/d)		**Feeding Guild** (food item)	**EDE** (mg a.i./kg bw)	**RQ**
Small Mammal (0.015 kg)				
Acute	<160.0	Insectivore (small insects)	438.78	**<2.74**
Reproduction	439.0	Insectivore (small insects)	438.78	1.00
Medium Sized Mammal (0.035 kg)				
Acute	<160.0	Herbivore (short grass)	1374.70	**<8.59**
Reproduction	439	Herbivore (short grass)	1374.70	**3.13**

Toxicity (mg a.i./kg bw/d)		Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Large Sized Mammal (1 kg)				
Acute	<160.0	Herbivore (short grass)	734.55	**<4.59**
Reproduction	439.0	Herbivore (short grass)	734.55	**1.67**

Table 17 Risk to Small Mammals - Lettuce

Risk to mammals was determined based on the acute EUP LD_{50} > 160 mg a.i./kg bw and reproductive NOEL = 439 mg a.i./kg bw, the use rate of 2240 g a.i./ha × 5, foliar DT_{50} = 10d^.

Toxicity (mg a.i./kg bw/d)		Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	<160.0	Insectivore (small insects)	153.95	<0.96
Reproduction	439.0	Insectivore (small insects)	153.95	0.35
Medium Sized Mammal (0.035 kg)				
Acute	<160.0	Herbivore (short grass)	482.32	**<3.01**
	<160.0	Herbivore (leafy foliage)	909.04	**<5.68**
Reproduction	439	Herbivore (short grass)	482.32	**1.1**
	439.0	Herbivore (leafy foliage)	909.04	**2.07**
Large Sized mammal (1kg)				
Acute	<160.0	Herbivore (short grass)	257.72	**<1.61**
	<160.0	Herbivore (leafy foliage)	485.73	**<3.04**
Reproduction	439.0	Herbivore (short grass)	257.72	0.59
	439.0	Herbivore (leafy foliage)	485.73	**1.11**

[1]) Endpoints were divided by an Uncertainty Factor to account for varying protection goals (i.e. protection at the community, population, or individual level).
[2]) EEC: For birds and mammals, the EEC takes into account the maximum seasonal cumulative rate on vegetation and is calculated using PMRA standard methods based on the Hoerger and Kenaga nomogram as modified by Fletcher (1994)
EDE = Estimated dietary exposure; calculated for each bird or mammal size based on the EEC on appropriate food item for each food guild (at the screening level, the most conservative EEC for each food guild was used). The EDE was calculated using the following formula: (FIR/BW) × EEC. For each body weight (BW), the food ingestion rate (FIR) was based on equations from Nagy (1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used; for mammals, the "all mammals" equation was used:
Passerine Equation (body weight ≤200 g): FIR (g dry weight/day) = 0.398(BW in g)$^{0.850}$
All Birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g)$^{0.651}$
All Mammals Equation: FIR (g dry weight/day) = 0.235(BW in g)0.822
[3]) RQ = exposure/toxicity; RQs < 0.1 were not calculated to show all decimal points
[4]) Conversion from a concentration (EEC) to a dose (EDE): [EDE (mg a.i./kg bw) = EEC (mg a.i./kg diet)/BW (g) × FIR (g et/day)] Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128.

Table 18 Toxicity Data Used to Derive the Species Sensitivity Distribution for Freshwater Algae

Species name	EC_{50} (mg a.i./L)
Sc. pannonicus	21.9
Anabaena flos aquae	7.24
Sc. subspicatus	6.14*
Navicula pelliculosa	6.12*
S. capricornutum	4.99

*: Geometric mean toxicity value

Results of SSD analysis for fosetyl-Al fungicide: Distributions were determined for freshwater algae. Acute EC_{50} values were used in the SSD as listed in Table 18. The most sensitive species is *S. capricornutum* with an EC_{50} of 4.99 mg a.i./L.

The HC_5 is 2.75 mg a.i./L (Table 19). Note that the confidence intervals on the fraction of species affected (FA) are relatively large, indicating high variability in the data set. For example, as a worst case scenario, up to 31.5% of all species could be affected at an EC_{50} level if exposed to a median HC_5 value of 2.75 mg a.i./L. Similarly, using the EC50 data set, the lower confidence interval of the HC_5 is 0.66 mg a.i./L, thus a 50% adverse effect could be observed in up to 5% of all plant species at this exposure level.

Table 19 Summary of Species Sensitivity Distribution Toxicity Data Analysis for Fosetyl-Al Fungicide

The HC_5[1] or the most sensitive endpoints are listed by taxonomic group*.

Test material	Exposure	Freshwater algae (mg a.i./L)
TGAI./EUP	Acute	[1]HC_5: 2.75 (from EC_{50})
		CI: 0.66-4.84 FA: 0.15-31.5%

(CI) = lower and upper confidence level of HC_5; (FA) = fraction of species affected; EUP = end-use product; *Where SSDs could not be determined, the most sensitive species endpoint value is reported; [1]Hazardous concentration to 5% of species;

Table 20 Risk to Aquatic Organisms – Spinach

EECs based on 7 × 3600g a.i./ha = 25200 g a.i./ha, 7 day interval, DT_{50} = 4.5d.

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
Freshwater Organisms						
Daphnia magna	Acute	TGAI: LC_{50}: 29.6 mg a.i./L H_3PO_3: LC_{50}: >29.7 mg/L	LC_{50} = 14.8 mg a.i./L H_3PO_3: LC_{50}: >14.8 mg/L	0.683 0.16	<0.1 <0.1	NO
	Chronic	21d-NOEC: 17 mg a.i./L	NOEC = 17 mg a.i./L	0.683	<0.1	NO
Grass shrimp	Acute	TGAI: LC_{50}: 3.6 mg a.i./L	LC_{50} = 1.8 mg a.i./L	0.683	0.37	NO
Rainbow trout	Acute: TGAI H_3PO_3	LC_{50} = 83.4 mg a.i./L LC_{50}: > 28.6 mg a.i./L	LC_{50} = 8.3 mg a.i./L LC_{50}> 2.86 mg a.i./L	0.683 0.16	<0.1 <0.1	NO
	Chronic	NOEC	NA		-	-
	ELS	28d-NOEC = 100 mg a.i./L	100 mg a.i./L		<0.1	NO
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	NOEC = 0.213mg a.i./L	0.683	**3.2**	**YES**
Amphibians (based on fish)	Acute	LC_{50} = 83.4 mg a.i./L	LC_{50} = 8.3 mg a.i./L	3.640	0.43	NO
	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L		**17**	**YES**
Aquatic vascular plants (*Lemna sp*)	Acute	TGAI: EC50: 79.7 mg a.i./L	EC50: 40 mg a.i./L	0.683	<0.1	NO
Algae Based on SSD	Acute	TGAI: HC_5 = 2.75 mg a.i./L	HC5 = 2.75 mg a.i./L	0.683	0.25	NO
Runoff (peak EEC value from use on spinach)						
Fathead	ELS	32d-NOEC =	NOEC = 0.213mg a.i./L	0.092E-3	<<0.1	NO

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
minnow		0.213mg a.i./L				
Amphibians (based on fish)	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L	0.49E-3	<<0.1	NO
Marine organisms: Screening level						
Saltwater invertebrates Eastern Oyster	Acute	TGAI EC50: 1.85	0.93 mg a.i./L	0.683	0.73	NO
	Chronic	NOEC	NA		-	
Saltwater fish Sheepshead minnow	Acute	TGAI LC_{50}: 122 mg a.i./L	LC_{50} = 12.2 mg a.i./L	0.683	<0.1	NO
	Chronic	NOEC	NA		-	
Saltwater algae *Skeletonema sp.*	Acute	EC50: 0.78 mg a.i./L	0.39 mg a.i./L	0.683	**1.75**	**YES**

* Uncertainty factor applied: [1]Estimated Environmental Concentration (EEC) in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80 cm deep water body / (EC50 ÷ 10 or LC_{50} ÷ 10); for a chronic exposure: RQ = EEC in an 80 cm deep water body / NOEC; for amphibians, the EEC in a 15 cm deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80 cm deep water body / (EC50 ÷ 2 or LC_{50} ÷ 2); for a chronic exposure: RQ = EEC in a 80 cm deep water body / NOEC
[3]Level of Concern (LOC) = 1 for aquatic organisms.

Table 21 Risk to Aquatic Organisms - Turf

EECs based on application to turf, 4 × 9600g a.i./ha = 38400 g a.i./ha, 14 day interval, DT_{50} = 4.5d.

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
Freshwater Organisms: Screening level						
Daphnia magna	Acute	TGAI: LC_{50}: 37 (29.6 a.i.) mg a.i./L H_3PO_3: LC_{50}: >29.7	LC_{50} =14.8 mg a.i./L H_3PO_3: LC_{50}: >14.8 mg/L	1.357 0.31	<0.1 <0.1	NO
	Chronic	21d-NOEC: 17 mg a.i./L	NOEC = 17 mg a.i./L	1.357	<0.1	NO
Grass shrimp	Acute	TGAI: LC_{50}: 3.6 mg a.i./L	LC_{50} = 1.8 mg a.i./L	1.357	0.74	NO
Rainbow trout	Acute: TGAI, H_3PO_3	LC_{50} = 83.4 mg a.i./L LC_{50}: > 28.6 mg a.i./L	LC_{50} = 8.3 mg a.i./L LC_{50}> 2.86 mg a.i./L	1.357 0.31	0.16 0.1	NO
	Chronic	NOEC	NA	-	-	
	ELS	28d-NOEC = 100 mg a.i./L	100 mg a.i./L	1.357	<0.1	NO
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	NOEC = 0.213mg a.i./L	1.357	**6.4**	**YES**
Amphibians (based on fish)	Acute	LC_{50} = 83.4 mg a.i./L	LC_{50} = 8.3 mg a.i./L	7.240	0.86	NO
	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L		**34**	**YES**
Aquatic vascular plants (Lemna sp)	Acute	TGAI: EC50: 79.7 mg a.i./L	EC50: 40 mg a.i./L	1.357	<0.1	NO
Algae Based on SSD	Acute	TGAI: HC_5 = 2.75 mg a.i./L	HC5 = 2.75 mg a.i./L	1.357	0.49	NO
Runoff (peak EEC value from use on turf)						
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	NOEC = 0.213mg a.i./L	0.046E-3	<<0.1	NO
Amphibians (based on fish)	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L	0.24E-3	<<0.1	NO

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
Marine organisms: Screening level						
Saltwater invertebrates Eastern Oyster	Acute	TGAI EC50: 1.85	0.93 mg a.i./L	1.357	**1.46**	**YES**
	Chronic	NOEC	NA		-	
Saltwater fish Sheepshead minnow	Acute	TGAI LC_{50}: 122 mg a.i./L	LC_{50} = 12.2 mg a.i./L	1.357	<0.1	NO
	Chronic	NOEC	NA		-	
Saltwater algae Skeletonema sp.	Acute	EC50: 0.78 mg a.i./L	0.39 mg a.i./L	1.357	**3.5**	**YES**

* uncertainty factor applied; [1]Estimated Environmental Concentration (EEC) in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80 cm deep water body / (EC50 ÷ 10 or LC_{50} ÷ 10); for a chronic exposure: RQ = EEC in an 80 cm deep water body / NOEC; for amphibians, the EEC in a 15 cm deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80 cm deep water body / (EC50 ÷ 2 or LC_{50} ÷ 2); for a chronic exposure: RQ = EEC in a 80 cm deep water body / NOEC
[3]Level of Concern (LOC) = 1 for aquatic organisms.

Table 22 Risk to Aquatic Organisms from Spray Drift – Spinach

EECs based on application to spinach, 7 × 3600g a.i./ha = 25200 g a.i./ha, 7 day interval, DT_{50} = 4.5d; ground boom sprayer, 6% drift 1m off field.

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
Freshwater Organisms						
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	NOEC = 0.213mg a.i./L	0.04	0.18	No
Amphibians (based on fish)	Acute	LC_{50} = 83.4 mg a.i./L	LC_{50} = 8.3 mg a.i./L	0.218	<0.1	NO
	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L		**1.0**	**YES**
Marine organisms						
Saltwater algae *Skeletonema sp.*	Acute	EC_{50}: 0.78 mg a.i./L	0.39 mg a.i./L	0.04	0.1	NO

Table 23 Risk to Aquatic Organisms from Spray Drift - Apples

EECs based on 4000 g a.i./ha 3 × = 12000 g a.i./ha, 42 day interval, $DT_{50\ aquatic}$ = 4.5d; airblast sprayer, 74% drift 1m off field.

Organism	Exposure	Endpoint (mg a.i./L)	Adjusted Endpoint* (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC exceeded?
Freshwater Organisms						
Fathead minnow	ELS	32d-NOEC = 0.213mg a.i./L	NOEC = 0.213mg a.i./L	0.5	**2.34**	**YES**
Amphibians (based on fish)	Acute	LC_{50} = 83.4 mg a.i./L	LC_{50} = 8.3 mg a.i./L	2.67	0.32	NO
	ELS	32d-NOEC = 0.213 mg a.i./L	NOEC = 0.213 mg a.i./L		**12.5**	**YES**
Saltwater algae *Skeletonema sp.*	Acute	EC50: 0.78 mg a.i./L	0.39 mg a.i./L	0.5	**1.28**	**YES**

Table 24 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Fosetyl-Al Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	<1 days (aerobic soil)
	Water	Half-life ≥ 182 days	3.5–4.5 days (aerobic water)
	Sediment	Half-life ≥ 365 days	Not available for this chemical
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilization is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure [1×10^{-10} Pa at 20 °C] and Henry's Law Constant (3.1×10^{-15} atm. $m^3 mol^{-1}$, $1/H = 7.69 \times 10^{12}$)
Bioaccumulation[4]	Log $K_{OW} \geq 5$		-2.1
	BCF ≥ 5000		NA
	BAF ≥ 5000		NA
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e. all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{OW}).

Appendix X Label Amendments for Commercial-class Products Containing Fosetyl-Al

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the following label statements. Please read each section carefully and make appropriate changes to your product labels.

The following uses are proposed for cancellation and all label directions relating to these uses would be removed from the appropriate labels:

- Drench application to bedding plants, and
- Use on cut flowers.

The following statements are proposed to be added under **PRECAUTIONS** to the appropriate labels:

> For airblast application, replace "hat" with "chemical-resistant headgear includes chemical-resistant Sou'Westers, chemical-resistant rain hat or large brimmed waterproof hat, and hood with sufficient neck protection".
>
> For mechanically pressurized hand gun application to blackberries, red/black raspberries, and strawberries: "Wear chemical-resistant coveralls when applying to blackberries, red/black raspberries, and strawberries using mechanically pressurized hand gun equipment."

To minimize public exposure to spray drift, the following statement is proposed to be added under **PRECAUTIONS**:

> "Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

The following statements are proposed to be added under **DIRECTIONS FOR USE** to the appropriate labels:

> "Do not apply this product using fogging equipment (handheld or automated), or using handheld mist blowers."
>
> "Not for use on cut flowers."
>
> "Not for use on other residential turf including residential lawns, gardens, playing fields, cemeteries, and schools."
>
> For use on blackberries, red/black raspberries and strawberries:

Wettable granule products
"For mechanically pressurized hand gun applications, use a spray volume of 250 – 1000 L water per hectare."

Wettable powder products
"For mechanically pressurized hand gun applications, use a spray volume of 300 – 1000 L water per hectare."

For use of wettable powder product(s) on turf at a rate of 16 kg a.i./ha, the following statement under APPLICATION RATE should be added:

"DO NOT handle more than 320 kg fosetyl-Al per person per day."

The following statements are proposed to be added under **DIRECTIONS FOR USE**:

"Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Boom height must be 60 cm or less above the crop or ground."

DO NOT apply by air.

Buffer zones:

Use of the following spray methods or equipment **DOES NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment and soil incorporation.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Table 1 Buffer Zones

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:				
		Aquatic Habitat of Depths:		Marine Habitat of Depths:		Terrestrial Habitat
		Less than 1 m	Greater than 1m	Less than 1 m	Greater than 1 m	
Field sprayer*	Spinach, red/black raspberries, blackberries, ginseng, highbush blueberries, strawberries, cranberries, ornamentals	1	1	1	0	0
	Cabbage, cole crops, rutabaga, lettuce, onions, tobacco	1	0	1	0	0
	Turf	2	1	1	1	0

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:				
		Aquatic Habitat of Depths:		Marine Habitat of Depths:		Terrestrial Habitat
		Less than 1 m	Greater than 1m	Less than 1 m	Greater than 1 m	
Airblast	Apples (early airblast)	15	0	1	0	0
	Apples (late airblast)	5	0	1	0	0
	Grapes (early airblast)	15	1	1	0	0
	Grapes (late airblast)	5	1	1	0	0

*For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

The following REIs (Table 2) are proposed to be added to the appropriate labels. Where deemed necessary, REIs are subdivided according to re-entry activities.

Table 2 Proposed Restricted-Entry Intervals

Crop	Activity	Proposed REIs (days)
Apples	Thinning	4
Blackberries, red/black raspberries	Irrigation	2
Brassica leafy vegetables (Chinese cabbage, broccoli, Brussels sprouts, cabbage, Chinese broccoli, Chinese mustard, cauliflower, kohlrabi)	Harvesting, hand	11
	Weeding, hand	9
	Scouting, topping, tying/training	9
Highbush blueberries	Irrigation (hand set)	3
Onions	Weeding, hand	8
Spinach	Irrigation (hand set)	4
Grapes	Harvesting, hand; Tying/training, leaf pulling	18
	Irrigation (hand set)	3
Table grapes	Girdling/turning	22
	Harvesting, hand; Tying/training, leaf pulling	15
Ornamental plants (nursery)	Irrigation (hand-set)	2

For remaining crops and postapplication activities, including those with longer REIs currently on labels: "Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours."

The following statements pertaining to the restricted-entry interval (REI) on turf are proposed under **DIRECTIONS FOR USE**:

Replace "Do not re-enter treated area until residues have dried." with "Do not enter treated golf course areas until residues have dried."

Add "For sod farms, do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours".

The following statement pertaining to the pre-harvest interval on brassica leafy vegetables is proposed under **DIRECTIONS FOR USE**:

"Observe a 7-day (11 days if hand harvest) PHI."

The following statements are proposed to be added under **ENVIRONMENTAL HAZARDS**:

"TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE."

"TOXIC to birds and small wild mammals."

"TOXIC to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland."

"To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application when heavy rain is forecast."

"Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body."

References

A. Information Considered in the Chemistry Assessment

List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
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1613307	2007, Fosetyl-Al Technical Material Manufactured - Description of Materials Used to Produce the Product and Description of Production Process - Codes AE F053616, RPA32545, LS74783, DACO 2.11.1, 2.11.2, 2.11.
1613308	Fosetyl-Al Technical Material - Discussion of the Formation of Impurities, DACO 2.11.4.
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B. Information Considered in the Toxicological Assessment

List of Studies/Information Submitted by Registrant

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PMRA Document Number	Reference
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Additional Information Considered

Published Information

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